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Pathology

EXPERIMENTAL PATHOLOGY

572. **Pathogenesis of Renoprival Cardiovascular Disease in Dogs**
W. J. KOLFF, I. H. PAGE, and A. C. CORCORAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 237–245, Aug., 1954. 5 figs., 27 refs.

It has been shown by Muirhead and Grollman (*Arch. Path.*, 1949, **48**, 234; *Abstracts of World Medicine*, 1950, **7**, 380) that dogs deprived of both kidneys may develop a " renoprival " condition characterized by hypertension, necrosis of the media of the arterioles in various sites, visceral haemorrhages, and myocardial lesions. In the present study, carried out at the Cleveland Clinic Foundation, Cleveland, Ohio, the authors kept nephrectomized dogs alive by peritoneal lavage or by means of the artificial kidney, and allowed them nourishment only in the form of glucose via the peritoneal fluid.

They found that minor increases in the water load did not influence the development of hypertension, but overhydration by injecting fluid equal in amount to 29% of the body weight led to a rise in blood pressure proportional to the rate and degree of overhydration. It was considered that overhydration was, however, a secondary factor, since in non-nephrectomized dogs in which the ureters had been transplanted to drain into the vena cava similar overloading did not produce hypertension. The authors postulate that a non-excretory function of the intact kidney protects against hypertension.

Serum sodium concentration was shown to be another contributory factor in the rise of blood pressure, but an increase in the sodium space and variations in the serum potassium level did not influence the blood pressure. In discussing the production of the vascular lesions the authors point out that although this is possible in nephrectomized dogs in the absence of increased blood pressure, arterial hypertension is a significant factor in the genesis of renoprival vascular disease (of which it is itself a concomitant) and the vascular lesions, which are usually proportional to its duration and intensity. Transection of the spinal cord at the level of C 6 in one dog did not prevent the development of renoprival disease.

It is suggested that the absence of protein from the diet of the animals may have accounted for the incidence of severe disease being lower than has been reported by other workers. *Thomas B. Begg*

573. **Vasomotor Nerve Stimulation and Mechanical Obstructive Factors in Renal Hypertension**
W. G. KUBICEK, F. J. KOTTKE, D. J. LAKER, and M. B. VISSCHER. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 246–250, Aug., 1954. 4 figs., 12 refs.

The study here reported from the University of Minnesota Medical School, Minneapolis, was originally designed to investigate the effect of chronic stimulation of the renal arteries and associated nerves on 2 dogs, but during the experiment the electrodes slipped and accidentally occluded the arteries, thus providing the additional opportunity to study the effects of mechanical obstruction.

In one dog drastic reduction in renal plasma flow and glomerular filtration rate, as measured by renal clearance of PAH and creatinine respectively, did not produce significant hypertension. But subsequent electrical stimulation of the renal pedicle at 3 volts and 2 c.p.s. for 20 hours per day for varying periods did produce hypertension for the duration of the stimulus. In the other dog stimulation produced reversible hypertension, but 7 months after the end of the experiment there was sustained elevation of the blood pressure and on stimulation of the splanchnic nerves a further rise occurred, which was at first reversible but later became permanent. In this animal the renal plasma flow and glomerular filtration rate were normal.

At necropsy the renal arteries were found to be partially occluded in the first dog and completely occluded in the second. Both animals had one atrophic and hypertrophied kidney, and a rich collateral circulation, especially to the larger kidney. On the basis of these findings the authors suggest that hyperactivity of the sympathetic nervous system superimposed upon a pathological process in the kidneys may be of importance in certain cases of clinical hypertension.

Thomas B. Begg

574. **Convulsive State Produced by Various Types of Shock. Conduct of Three Barriers (Blood–Aqueous, Blood–Labyrinthine Fluids, and Blood–Liquor [Spinal Fluid]) with Reference to Some Convulsive States**
R. FREGNI and A. DE POLI. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **60**, 149–153, Aug., 1954. 2 figs., 5 refs.

It has been shown that a convulsant dose of pentylenetetrazole (leptazol, " cardiazol ") increases the permeability of the encephalon to procaine, but that this increase does not occur after electric shock. Working

at the University of Milan, the authors investigated the changes, if any, in permeability of the barriers between the blood and the aqueous humour, the cerebrospinal fluid, and the labyrinthine fluid in guinea-pigs subjected to electric shock and to shock produced by the injection of pentylenetetrazole and acetylcholine. The degree of permeability was measured by estimating the amount of injected fluorescein sodium passing between the blood and the respective fluids in a certain time.

Acetylcholine in convulsant doses had the greatest effect on the permeability of the barriers; one hour after its administration the fluorescein content of the aqueous humour was six times greater than that in the control animals, while in the labyrinthine fluid (endolymph) the content was three times greater in the treated animals; permeation into the cerebrospinal fluid was considerably less. The effect of pentylenetetrazole was similar to that of acetylcholine, but not so marked. Electric shock caused little alteration in the permeability of the barriers. In discussing these findings the authors agree that the vascular endothelium is the principal structure concerned in maintaining the barriers, although possibly other factors may be involved. Certainly the pressure in the capillaries is important, and some workers believe that the extent of the capillary bed is altered by relaxation of the precapillary vessels which, under the influence of adenosine triphosphate, have been shown to act as sphincters. In the convulsive state there is a " vascular storm " producing rapid changes in vascular calibre, especially in the cerebral regions. The authors conclude that their experiments seem to show that the permeability of the barriers varies with the intensity of the vascular changes following shock rather than with the convulsive state, and that acetylcholine may play a special part in relaxing the precapillary sphincter.

F. W. Watkyn-Thomas

CHEMICAL PATHOLOGY

575. **The Production of Gamma-globulin in the Central Nervous System**

E. O. FIELD. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 228–232, Aug., 1954. 3 figs., 16 refs.

At the Middlesex Hospital, London, and the Radcliffe Infirmary, Oxford, the total and differential protein contents of the serum and cerebrospinal fluid were determined in 4 normal subjects, in 3 cases of multiple myelomatosis, 26 of disseminated sclerosis, 2 of neurosyphilis, and in 4 normal Mantoux-positive subjects receiving intrathecal tuberculin. The serum total protein content was determined refractometrically, and the cerebrospinal-fluid protein value by this method or by turbidometry or the micro-Kjeldahl technique. Protein fractions were determined by electrophoresis, the cerebrospinal fluid being concentrated when necessary by dialysis against 50% gum arabic.

The ratio of albumin to γ globulin was calculated for both serum (Rs) and cerebrospinal fluid (Rc) and these values compared. The mean value of Rs/Rc was 0·87 for the 4 normal subjects, 0·31 for the cases of multiple myeloma, and ranged from 0·98 to 2·0 for the other cases. The normal value of Rc averaged $6{\cdot}2\pm4$ and ranged from $2{\cdot}4\pm1$ to $3{\cdot}9\pm1$ in the cases of disseminated sclerosis. In the cerebrospinal fluid (C.S.F.) the $(\alpha+\beta)$-globulin value correlated well with the albumin content (correlation coefficient 0·76), but the γ-globulin value less so (correlation coefficient 0·50). The author suggests that the α- and β-globulin fractions in the C.S.F. are derived entirely from the serum proteins, but the γ-globulin fraction only partially from this source, the increase in the value of Rs/Rc observed in disseminated sclerosis resulting from the production of γ globulin in the central nervous system in this disease. It is further suggested that the source of the γ globulin may be the lymphocytes in the C.S.F., since the Rc value in general varied inversely as the cell count. This thesis is supported by the findings in the patients receiving tuberculin intrathecally, in whom Rc fell during the period in which the lymphocyte count of the C.S.F. rose.

M. Lubran

576. **An Improved Method for the Determination of Proteolytic Enzymes in Duodenal Contents for the Purpose of Testing Pancreatic Function.** (Eine für die Zwecke der Pankreasfunktionsprüfung verbesserte Methode zur Bestimmung der proteolytischen Fermente im Duodenalinhalt)

E. BALZER and K. WERNER. *Gastroenterologia* [*Gastroenterologia* (*Basel*)] **82**, 1–9, July, 1954. 2 figs., 21 refs.

After briefly discussing the shortcomings of von Leubner's and the haemoglobin proteolysis methods of estimating the proteolytic activity of duodenal contents, the authors describe their own titrimetric technique, which they have developed from von Leubner's method at the University Medical Clinic, Münster. They use 10 ml. of a 5% solution of casein—a protein which is split by trypsin but not by peptidase—to which is added 0·5 ml. of duodenal contents and 2 ml. of a buffer solution. After 90 minutes in a water-bath at 38° C. 10 ml. of formol neutralized with sodium hydroxide is added and the whole titrated with N/10 sodium hydroxide solution, using phenolphthalein as the indicator. A graph relating the amount of alkali used in the titration to the amount of pancreatic protease present in the specimen of duodenal juice is presented, and shows that, in contrast to the original Leubner method, the authors' technique enables amounts of less than 2 mg. of protease to be accurately estimated, 2 mg. of protease corresponding to 4 ml. of NaOH solution. Indeed, the sensitivity of the new method is at its highest with such small amounts, and it may therefore be used for the quantitative assessment of degrees of pancreatic hypofunction. The slope of the curve remains sufficiently steep for accurate estimations throughout the normal range and well above it.

In the second half of the paper examples are given of titrations carried out on duodenal contents from healthy individuals and patients with pancreatic disease. One patient with almost complete absence of pancreatic acinar secretion excreted in his faeces only 10% of his dietary protein; this shows that unlike absence of pan-

creatic lipase, which causes a marked increase in faecal fat content, absence of trypsin does not necessarily result in failure to absorb protein. *Ferdinand Hillman*

577. **A New Test of Pancreatic Function Based on Starch Tolerance**

T. L. ALTHAUSEN and K. UYEYAMA. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 563–575, Sept., 1954. 4 figs., 12 refs.

The authors, working at the University of California School of Medicine, San Francisco, have devised a test which is intended to provide a measure of the amylolytic activity of the pancreatic juice in the intestines. A solution of 100 g. of soluble starch in 450 ml. of water is administered to the fasting subject, the blood sugar level being determined before, and ½, 1, 2, and 3 hours after, giving the starch. The starch must be in the form of a hot gelatinous mass, as otherwise even in normal subjects the rise in blood sugar level may be only slight. Also the starch solution must at no time be boiled, or an apparently normal result may be obtained in cases of pancreatic disease. Moreover, patients with a disorder of the pancreas, even in the absence of clinical diabetes, often have a reduced glucose tolerance, which would unavoidably increase the height of the blood sugar curve after starch administration. To arrive at a correct answer, therefore, it is necessary to determine, in addition, the glucose tolerance curve following the ingestion of 100 g. [!] of glucose, the extent to which the maximum blood sugar level attained after taking glucose exceeds that attained after taking starch being calculated as a percentage of the latter and compared with the normal range, which in 27 patients without diseases of the pancreas was from −42·3% to +70·3%. In a group of 23 cases of chronic pancreatitis the result of the test was above the upper limit of normal in all but 2 cases, the highest value obtained being +590%, while of 10 cases of suspected pancreatic disease the result was over +70% in 8 and over +100% in 5.

[Although all these precautions are doubtless necessary, the authors found in fact that the majority of patients with pancreatic disease gave a flat blood sugar curve after ingestion of starch as compared with control subjects.] *H. Lehmann*

578. **Serum Cholinesterase Activity in the Normal Individual and in People with Liver Disease**

K. KAUFMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 533–545, Sept., 1954. 38 refs.

Serum cholinesterase activity is measured by adding 0·2 ml. of the serum or plasma to 20 ml. of 0·01 M solution of acetylcholine previously adjusted with 0·1 N sodium hydroxide solution to *p*H 8. The mixture is kept at 30° C. for 30 minutes and the *p*H is maintained at a constant level by titrating every 5 minutes with 0·1 N NaOH solution. The higher the cholinesterase activity of the serum, the more acetic acid will be formed from acetylcholine and the greater will be the amount of alkali needed to neutralize it. Hence the number of millilitres of 0·1 N NaOH solution used during the test gives a measure of the enzyme activity, the normal range being from 1·00 to 3·27 ml. The same technique may be employed, with suitable modifications, to measure the cholinesterase activity of the erythrocytes.

The measurement of serum cholinesterase activity has been found by the author to be a valuable and reliable test of liver function and for following the process of recovery from hepatitis and other liver disorders. In particular, he finds it useful in the differential diagnosis of jaundice. [As liver function may be damaged even in cases of extra-hepatic obstruction if the disease is prolonged, this application of the test should be restricted to cases of recent jaundice.] The interesting observation is recorded that a transient rise in serum cholinesterase activity occurs after operations; this is considered to be due to flooding of the blood with the enzyme from liver cells damaged by the anaesthetic used.

H. Lehmann

579. **Maximum Urine Concentration**

B. E. MILES, A. PATON, and H. E. DE WARDENER. *British Medical Journal* [*Brit. med. J.*] **2**, 901–905, Oct. 16, 1954. 4 figs., 9 refs.

At St. Thomas's Hospital, London, the authors have studied the errors involved when specific gravity, as measured by a standard hydrometer, is used as an approximate indication of the osmolarity of urine. They conclude from their findings that the specific gravity of urine may give a grossly misleading idea of its osmolarity (as measured by a cryoscopic method), the presence of heavy molecules such as those of sugar or protein giving disproportionately high specific-gravity readings. Moreover, inaccuracy may arise from the errors of calibration commonly found in hydrometers and from variations in the temperature of the urine.

They also investigated the effect of water deprivation for various periods on the osmolarity of the urine and compared the maximum osmolarity obtainable in this way with that obtainable by giving "pitressin tannate" to normal subjects and patients with renal disease. A group of 13 convalescent patients with normal renal function were deprived of fluid for 30 hours, though they were allowed normal food, and the osmolarity of 4-hourly urine samples collected during the last 20 hours of the experiment determined. It was found that the maximum osmolarity was rarely reached after 14 to 18 hours' deprivation of water, and the authors suggest that deprivation for at least 22 hours is necessary if a reasonably accurate idea of maximum osmolarity is to be obtained. It was also observed that the osmolarity of the urine did not always increase steadily to a maximum, and in some cases considerable fluctuation occurred. From another group of 19 patients with a variety of diseases (including chronic nephritis in 4 cases), who were either convalescent or in a steady clinical state, three specimens of urine were collected at 4-hourly intervals between 8 a.m. and 8 p.m. on two separate occasions —on the first occasion after 24 to 36 hours' water deprivation, and on the second after a subcutaneous injection of 5 units of pitressin tannate in oil had been given at 7 a.m. The subjects were arbitrarily divided into those who, on deprivation of water, could concentrate their urine above an approximate level of

850 m. osmols per litre and those who could not. Among the former the effect of pitressin was conspicuously less than that of water deprivation, whereas in the latter group it was as good or even better.

Further experiments on 4 normal subjects showed that the osmolarity of the urine depended, among other factors, on its urea content, tending to be higher at any given rate of solute output when the concentration of urea was above average. The authors suggest that if this is due to partial permeability to urea of the cells at the most distal site of tubular reabsorption, then the specific gravity may fortuitously be a better indication of "effective" osmolarity (as regards the tubule cells) than it is of the total osmolarity of the urine, because when the urea concentration is high the specific gravity is relatively low. *M. J. H. Smith*

HAEMATOLOGY

580. **A Study on the Occurrence of Platelet Antibodies.** [In English]
A. J. SAUER and J. J. VAN LOGHEM. *Vox Sanguinis* [*Vox Sang.* (*Amst.*)] **4**, 120–128, Sept., 1954. 1 fig., 29 refs.

In the study here reported from the Netherlands Red Cross Blood Transfusion Service, Amsterdam, the haemagglutination reaction of "tanned" erythrocytes (that is, erythrocytes treated with tannic acid) coated with platelet antigens, as described by Kissmeyer-Nielsen (*Vox Sang.* (*Amst.*), 1953, **3**, 123) was applied to samples of serum from 55 patients with idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, and similar conditions, and to 35 normal control sera. When native serum was used the results were equivocal, but with heated serum 17 out of the 55 specimens from patients (31%) and only 2 out of the 35 control specimens (5·6%) gave positive results. The authors consider that the haemagglutination technique may be of value in the study of platelet antibodies. *A. Brown*

581. **An Abnormal Substance Present in the Erythroblasts of Thalassaemia Major. Cytochemical Investigations.** [In English]
G. ASTALDI, E. G. RONDANELLI, E. BERNARDELLI, and E. STROSSELLI. *Acta haematologica* [*Acta haemat.* (*Basel*)] **12**, 145–153, Sept., 1954. 3 figs., bibliography.

In a study carried out at the University of Pavia the authors subjected the erythroblasts of peripheral blood and bone marrow from 20 cases of thalassaemia major to numerous staining reactions, including the periodic-acid–Schiff (P.A.S.) reaction.

A substance giving a P.A.S.-positive reaction was constantly found in a number of erythroblasts from both blood and marrow in all 20 cases. Cytochemical tests of this substance lead the authors to believe that it is a gluco- or muco-protein or a neutral mucopolysaccharide. Such a substance was not found in the embryonic erythroblasts of premature infants, indicating that there is probably no relation between this substance and the "foetal" haemoglobin of thalassaemia. Nor did the P.A.S. test reveal its presence in the erythroblasts of patients with various anaemias and leukaemias, except in one case of chronic myeloid leukaemia; in this case further cytochemical studies, however, showed the P.A.S.-positive substance to be unlike that found in the cases of thalassaemia. No P.A.S.-positive erythroblasts were found in the bone marrow in 10 cases of thalassaemia minima.

The authors therefore consider that the erythroblasts of patients with thalassaemia major contain a specific substance which is either a gluco-mucoprotein or a neutral mucopolysaccharide, and which is not present in the normal "erythron". *A. J. Duggan*

582. **The Significance of Proplasmocytes and Atypical Plasma Cells in the Benign Lymphocytic Meningitis Syndrome**
P. WOLF. *Blood* [*Blood*] **9**, 971–976, Oct., 1954. 2 figs., 7 refs.

The author considers that examination of the blood may help in differentiating tuberculous meningitis from other forms of lymphocytic meningitis, especially in the difficult cases in which no tubercle bacilli are found in smears of deposit from the cerebrospinal fluid and the spinal-fluid sugar content is low.

In illustration of this he reports the findings in 10 cases of non-tuberculous benign lymphocytic meningitis admitted to Crumpsall Hospital, Manchester, in all of which the total leucocyte count was low, the number of polymorphonuclear leucocytes was relatively reduced, and, most important, plasma cells appeared in the blood in 9 out of the 10 cases; these plasma cells were mostly atypical early forms, but in 2 cases typical plasma cells were present as well. In contrast, no plasma cells were found in the peripheral blood smears of 12 patients admitted with proved tuberculous meningitis. The benign meningitis was not of the same form in all the 10 cases, the complement fixation test for lymphocytic choriomeningitis being positive in only 4 cases; but clinically the cases were very much alike. The author shows that a similar blood picture may occur in other virus diseases, but not in tuberculosis, and therefore its demonstration is a useful additional diagnostic pointer.
M. C. G. Israëls

583. **An Unidentified Reticuloendothelial Cell in Bone Marrow and Spleen. Report of Two Cases with Histochemical Studies**
A. SAWITSKY, G. A. HYMAN, and J. B. HYMAN. *Blood* [*Blood*] **9**, 977–985, Oct., 1954. 4 figs., 16 refs.

The finding independently by two workers (at the Presbyterian Hospital and at Queens General Hospital, Jamaica, New York, respectively) of a hitherto unidentified cell in the spleen and bone marrow of 2 patients led to an investigation of its characteristics and possible significance. This cell was a large phagocytic reticuloendothelial cell, the cytoplasm of which was shown by Wright's stain to be packed with blue-staining, pigmented granules of various sizes. Histochemical studies showed that the granules contained mucopolysaccharides, but no fat, glycogen, nucleoprotein, or alkaline phosphatase. Both patients had a

symptomless hepatosplenomegaly. In one case only a few cells were found in the marrow and none in a liver biopsy specimen; in the other the cells were relatively frequent in the marrow and were also found in material from splenic puncture; a lymph-node biopsy specimen from this patient showed central caseation with a rim of these unidentified phagocytic cells. Somewhat similar cells were described by Moeschlin in 1947. The authors are unable to ascribe any function or diagnostic significance to the cells, but hope that other workers will look out for them. *M. C. G. Israëls*

MORBID ANATOMY AND CYTOLOGY

584. **Metastasis of Neoplasms to the Central Nervous System and Meninges**

S. Lesse and M. G. Netsky. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **72**, 133–153, Aug., 1954. 15 figs., 15 refs.

During the period 1938–47, 595 complete necropsies were carried out at the Montefiore Hospital, New York, on patients dying of cancer. Metastatic lesions in the central nervous system (C.N.S.) or meninges were found in 207 (35%) of these cases and an analysis of the findings is presented here. Most of the 207 patients were between 40 and 50 years old, but one was 4½ and another 76; 124 were female and 83 male, the predominance of females being accounted for by the large number of patients with mammary carcinoma. Among the 229 patients in the whole series with primary carcinoma of the lung the sex incidence was in the ratio of 3·4 men to one woman, whereas among the 50 with metastases in the C.N.S. or meninges the ratio was 2 men to one woman. It would thus appear that pulmonary neoplasms are more prone to metastasize to the C.N.S. in women than in men; this may be due in part to the greater relative frequency of adenocarcinomata in women and of squamous-cell carcinomata in men.

The interval between clinical onset of primary and secondary growths was slightly more than a year in most cases. In 10%, however, C.N.S. metastases provided the first clinical evidence of neoplasia, while in one case of mammary carcinoma the interval was 16 years. In as many as 32% of cases the C.N.S. metastases were asymptomatic, dural metastases being more frequently clinically silent than intracerebral deposits. Those patients who did develop symptoms rarely lived more than a few months after their onset. Headache—usually generalized and sometimes unrelated to increased intracranial pressure—was especially common and frequently early. Other very common symptoms were disturbances of personality and intellect and motor weakness, the former being most often associated with parenchymal rather than meningeal involvement. Likewise, seizures and evidence of pyramidal-tract involvement were commoner in those with parenchymal tumours.

Primary tumours of the breast and lung accounted for more than half the cases of metastasis in the C.N.S., whereas tumours of the gastrointestinal tract, ovary, pancreas, and genito-urinary system—with the exception of the kidney and prostate—rarely gave rise to such metastases. When the primary tumour was in the lung, kidney, or thyroid gland, or when it was sarcomatous, the metastases were most commonly parenchymatous, the parietal and frontal lobes being involved most often. Meningeal involvement was more common in cases of prostatic carcinoma, multiple myeloma, malignant lymphoma, and leukaemia. Solitary metastases were seen on 25 occasions, 8 of them being cerebellar, and were most commonly associated with those tumours which metastasize most frequently to the brain and not, as is held by some authorities, with those from the kidney.

The macroscopic and microscopic appearances are described in detail. Of the secondary carcinomata, more than half were acinar and about one-third were anaplastic, only 12% being of the squamous-cell type, the lung being the only common source of these. In 77% the degree of differentiation of the secondary was similar to that of the primary tumour. *Adrian V. Adams*

585. **Fusiform Swellings on the Terminal Portions of Peripheral Nerves**

H. W. Daniell. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **13**, 467–475, July, 1954. 9 figs., 9 refs.

"Gangliform" or "fusiform" swellings on the peripheral nerves are most commonly seen at the wrist, on the dorsal interosseous branch of the radial nerve, but they also occur, though not so prominently, at other sites. The author dissected out the lateral branch of the deep peroneal nerve in 20 routine necropsy subjects and found fusiform swellings on this nerve in 7. In 11 of the 20 cases a portion of the medial branch of the same nerve was removed, and a fusiform swelling was discovered on one of these. Two more specimens of fusiform swellings were obtained from the dorsal interosseus nerve, and one from the medial plantar nerve. The position of the swelling on the lateral branch of the deep peroneal nerve was constant, being always in relation to the lateral portion of the dorsal surface of the navicular bone, and the author points out that at this point the nerve is especially subject to chronic irritation from pressure and friction—to which, he concludes, these swellings are due both in this and other situations in the body.

A detailed histological examination was made of each fusiform swelling. Changes were present in the extraperineural tissue, in the perineurium, and in the intrafunicular connective tissue. Fibrosis of the extraperineural tissue was observed to some extent in nearly all the specimens, varying in degree from lamellation around the individual funiculi to masses of dense fibrous tissue surrounding the whole group of funiculi. In the perineurium there was wide variation in the relation of the thickness of the perineurium to the diameter of the funiculus it surrounded, the former ranging from $\frac{1}{45}$ to $\frac{1}{2}$ of the latter. Intrafunicular changes were also variable. Most of the funiculi exhibited a diffuse increase in fibrous tissue, with an increased vascularity in many cases. The most characteristic lesion, however, was the formation of

large, hyalinized, fibrous bodies, which occurred mainly in the connective tissue separating large groups of funiculi. These fibrous bodies appeared to be composed of two distinct parts—a central fibrous core consisting of a ring of cells resembling a small arteriole filled with collagenous material, and a surrounding mass of fibrous tissue arranged in concentric layers. In the largest fibrous bodies (which were assumed to be of longer standing) degeneration of the core had occurred and it had become replaced by a whorled pattern of anuclear fibrous tissue. In serial section many of these fibrous bodies were found to be cigar-shaped.

[These histological characteristics of the fusiform swellings are well displayed in photomicrographs, with which the article is lavishly illustrated.]

Ruby O. Stern

586. **Cytologic Studies of Cell Suspensions with Special Reference to Neoplasms**

J. B. HAZARD. *Laboratory Investigation* [*Lab. Invest.*] 3, 315–336, Sept.–Oct., 1954. 11 figs., 20 refs.

The author describes a method used at the Cleveland Clinic Foundation, Cleveland, Ohio, by which unfixed, fresh suspensions of tumour cells are stained with a solution of toluidine blue or of neutral red in serum, and examined wet. The cytological appearances obtained are distinct and distinctive. Using this method he has examined 95 specimens of tumour scrapings, 260 specimens of fluid from serous cavities, 40 of cerebrospinal fluid, 602 of bronchial washings, and a few specimens of urine and sinus washings. In all cases his conclusions agreed with those formed from examination of fixed films from the same material. The method was especially valuable in the evaluation of tumours of the central nervous system. The majority of malignant cells failed to localize neutral red. The advantages of the method, such as ease of preparation and absence of cell distortion and of artefacts, far outweigh the disadvantages, the chief of which of course is the impermanence of the specimen. *J. B. Enticknap*

587. **Identification of Types and Primary Sites of Metastatic Tumors from Exfoliated Cells in Serous Fluids**

N. C. FOOT. *American Journal of Pathology* [*Amer. J. Path.*] 30, 661–677, July–Aug., 1954. 28 figs., 8 refs.

Working at Cornell University Medical College, New York, the author has investigated the problem of whether, by examination of exfoliated malignant cells, the site and type of the primary tumour can be deduced with any degree of accuracy. To this end he has examined in detail the cellular components in 219 specimens of malignant serous effusions from the pericardium, pleural cavity, and the peritoneum. By working out group characteristics he was able to locate the site of the primary lesion with a degree of accuracy for the most frequently encountered neoplasms, which varied from 50% for intestinal carcinoma to 77% in cases of bronchogenic carcinoma.

In carcinoma of the breast malignant cells were usually not numerous in the smears; when present they were rather large and spheroidal, and arranged not infrequently in large clumps due to multiplication of the cells in the fluid, to which the author applies the term " proliferation spheres ". Occasionally abortive tubules were met with. The cellular exudate consisted chiefly of lymphocytes and histiocytes. In bronchogenic carcinoma multinucleation of the rather large, but not numerous, malignant cells was a distinct feature, and the cells tended to form small clumps composed of from 3 to 8 cells. Pus cells were present more often in this group than in any of the others, presumably owing to secondary infection of broken-down cancerous lung. In ovarian carcinoma the cells were usually numerous, large, spheroidal, and lying either discretely or in dense clumps in which their outline was so indistinct as to give them a syncytial appearance. Frequently the cell membrane displayed a double contour, and the cytoplasm was pale, clear, and conspicuously vacuolated, while the nuclei were oval and sharply defined. Proliferation spheres were present in about one-third of these smears, but were less concentrically arranged than in those from carcinoma of the breast. Inflammatory cells were usually represented by lymphocytes and histiocytes.

In gastric carcinoma malignant cells were usually so few that they could be demonstrated only with difficulty. They were small and usually spheroidal; slender, fusiform cells, if present, were very suggestive of a gastric origin. Cell clusters were small and less numerous than in smears from other tumours. Lymphocytes and histiocytes were the common non-neoplastic elements. In smears from tumours of lymphoid tissue the cells were extremely numerous and pleomorphic, the latter quality differentiating them from simple inflammatory processes, while the presence of eosinophils among them allowed of a tentative diagnosis of Hodgkin's disease; the characteristic giant cells of the latter condition were not encountered in the exudates. Determination of the nature and site of other malignant tumours proved to be impossible; for example, in 2 cases of malignant melanoma in the series the cells were so devoid of pigment that the diagnosis was missed.

The author concludes that as a careful analysis of the cellular characteristics of malignant serous effusions, combined with the essential clinical data, will allow of an accurate diagnosis in 65 to 76% of cases of the more common tumours, this method is worthy of a fair trial.

R. Salm

588. **Mucus-secreting Cells in Colloid Cysts of the Third Ventricle**

W. H. MOSBERG and W. BLACKWOOD. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] 13, 417–426, July, 1954. 1 fig., bibliography.

The authors here report histological observations made on 14 cases of colloid cyst of the third ventricle. An exhaustive review of 105 similar cases reported in the literature provides many points of interest, of which a noteworthy one is that in only one of these cases did the lining epithelium or contents of the cyst stain positively with mucus-specific stains. This finding is in sharp contrast to the authors' own observations. Of their 14 cases, 7 were available for staining with mucicarmine

and in 6 a positive result was obtained either in the lining cells or in the cyst contents. After a discussion of the pathogenesis of these colloid cysts and a reference to the varied nomenclature which has been applied to them, the authors conclude that the location of the cysts almost invariably in the midline—and nowhere else in the brain—is a strong point in favour of their origin from an embryonic remnant rather than from the choroid plexus. *Ruby O. Stern*

589. **Morbid Anatomy of Tuberculous Lesions after Chemotherapy.** (Étude anatomique des lésions tuberculeuses traitées par les antibiotiques)
J. DELARUE, J. PAILLAS, G. GOUYGOU, L. BOCQUET, S. BOUHEY, and G. CHOMETTE. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **18**, 481–507, 1954. 10 figs., 16 refs.

This paper from the Morbid Anatomy Laboratories of the Faculté de Médecine de Paris gives a description of the effects of streptomycin, PAS, and isoniazid, singly and in combination, on tuberculous lesions of the lung, kidney, synovial membranes, meninges, and other tissues. The material examined included 80 surgical specimens of the lung, serial biopsy specimens from 11 patients with tuberculous arthritis, surgical specimens of kidney tissue, and various specimens of tissue removed post mortem in cases of tuberculous meningitis and other conditions. Sections were stained with haematoxylin–eosin–saffranin, Masson's trichome stain, and Wilder's silver stain; they were also stained by the Ziehl–Neelsen method.

The authors conclude from their findings that the drugs used accelerate healing, but produce no specific morphological changes of major degree in the tuberculous lesions. The earliest ("exudative") lesions respond best to treatment, miliary lesions becoming fibrosed, while caseous lesions are more rapidly walled off by fibrous tissue, but not more rapidly absorbed. Pulmonary cavities are more frequently lined by epithelium after chemotherapy, and tuberculous follicles tend to lose their characteristic appearance, becoming changed into lymphoid nodules with a few giant cells in their centre and perhaps showing some fibrosis. Caseous foci and lymphoid follicles may be seen in the meninges in cases of tuberculous meningitis after chemotherapy, whereas in untreated cases these lesions are never seen, death occurring too early in the course of the disease for them to be formed. *A. Wynn Williams*

590. **Histological Studies of Pelvospondylitis Ossificans (Ankylosing Spondylitis) Correlated with Clinical and Radiological Findings**
B. ENGFELDT, R. ROMANUS, and S. YDÉN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 219–228, Sept., 1954. 7 figs, 15 refs.

As a result of their clinical and radiological studies of some 130 cases of ankylosing spondylitis at Karolinska Sjukhuset, Stockholm, the authors offer a new and more coherent concept of this disease, for which, they propose, the findings suggest the more descriptive designation of "pelvospondylitis ossificans". Early changes consist in inflammatory decalcification, bone resorption and destruction, and possibly a reactive sclerosis in the adjacent tissues. This is followed by a reparative phase, with proliferation, ossification, and reconstruction, but both phases may be present concurrently in different parts of the sacroiliac joints. They note that chronic non-specific infection of the prostate and particularly of the seminal vesicles is present in most cases of this disease in men, and suggest that spread occurs by the so-called vertebral venous system. Also, examination of the lower lumbar disks by discography (30 cases) showed progressive narrowing of one or more of the intervertebral spaces, and in some cases evidence of rupture or prolapse of the disk.

These findings, the authors consider, explain a number of hitherto obscure features in pelvo-spondylitis, such as its predominance in males with onset in early adult life, the concurrence of dysenteric upsets, and the association of similar skeletal changes in patients with brucellosis or paraplegia. *A. C. Lendrum*

591. **Allergic Prostatitis in Asthmatics**
M. J. STEWART, S. WRAY, and M. HALL. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 423–430, 1954. 7 figs., 10 refs.

The authors describe 2 cases of prostatic urinary obstruction in asthmatics in which histological examination of the removed prostatic tissue revealed a picture typical of some well-established allergic conditions. The first patient, aged 61, was subjected to prostatectomy and remained free both from urinary symptoms and from asthma 7 years after the operation. The second patient, aged 49, on whom perurethral resection was performed, also made a good recovery.

Two distinct cellular reactions of the type seen elsewhere in the body in polyarteritis nodosa and rheumatic carditis were evident. The first consisted of focal granulomata with central fibrinoid necrosis and occurred in relation to the unstriped muscle, while the second was a much more widespread eosinophilic infiltration. The urethral mucosa showed only slight eosinophilia and no granulomata.

The authors quote 3 cases from the American literature in which the findings were closely similar. They suggest that the urine of asthmatics who develop prostatic symptoms should be examined for eosinophiluria. *W. Skyrme Rees*

592. **Observations on the Pathology of Sjögren's Syndrome**
B. S. CARDELL and K. J. GURLING. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 137–146, 1954. 6 figs., 12 refs.

593. **The Insular Tissue in Fibrocystic Disease and Morphologically Related Conditions of the Pancreas.** (Über den Inselapparat bei cystischer Pankreasfibrose und morphologisch verwandten Zuständen des Pankreas)
H. MEISSNER. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **114**, 192–211, 1954. 6 figs., 44 refs.

Bacteriology

594. Disadvantages of the Rectal Swab in Diagnosis of Diarrhoea

M. E. M. THOMAS. *British Medical Journal* [*Brit. med. J.*] 2, 394–396, Aug. 14, 1954. 23 refs.

The author, writing from the Public Health Laboratory, Edmonton, London, recognizes the undoubted value of the rectal swab in certain types of investigation, but advances reasons why whole faeces and not rectal swabs should be the specimens of choice in the diagnosis of diarrhoea. The chief of these is that a swab specimen precludes any macroscopical, microscopical, or chemical examination of the faeces. Of a series of 3,183 specimens of faeces examined at the laboratory, 20% showed abnormalities such as the presence of parasites, pus, fat, and fresh or occult blood, which could not have been demonstrated in rectal-swab specimens. Moreover, the rectal-swab method is less reliable in making a bacteriological diagnosis. During an epidemic of Sonne dysentery it was repeatedly observed that cultures from swabs were negative, although *Shigella sonnei* was isolated from faeces from the same patient, sometimes on the same day. Further, in no case did the swab specimen yield a positive culture when the culture of faeces was negative. Again, swabs collected in general practice are subject to delays in transit to the laboratory, and the partial drying which ensues has a lethal effect on some pathogenic bacilli. Lastly, the use of selective media, which facilitate the finding of scanty bacilli by the culture of faecal samples very much larger than can be collected on a swab, has greatly improved cultural results.

E. G. Rees

595. A Cytochemical Study of *Entamoeba histolytica*

H. N. RAY and P. C. SEN GUPTA. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] 23, 529–533, Sept., 1954. 2 figs., 12 refs.

The authors, at the Calcutta School of Tropical Medicine, determined by standard cytochemical methods the presence and distribution of certain substances in amoebae and cysts of *Entamoeba histolytica*.

The presence of mitochondria and the Golgi complex was demonstrated in the endoplasm of amoebae. The rod-shaped mitochondria and the spheroids which comprised the Golgi complex were not fixed in position, but in active amoebae were swept along in the protoplasmic stream. Fat was distributed in the endoplasm in the form of fine droplets, while glycogen was present as a finely granular or hyaline mass. In precystic amoebae a large hyaline mass of glycogen was seen close to the nucleus.

Alkaline phosphatase was found to be present mainly in the nuclei of amoebae and cysts, both the peripheral chromatin and karyosome containing this enzyme. The cytoplasm exhibited a distinct but much weaker reaction, the ectoplasm sometimes being stained only at the inner and outer margins. In a mature cyst the enzyme was detected on the wall where a minute depression indicated the possible presence of a micropyle. The chromatoid bars gave a faint reaction.

Acid phosphatase in amoebae was similar in distribution to alkaline phosphatase, in that the nucleus gave a strong reaction whereas the endoplasm gave only a faint reaction. However, acid phosphatase was not observed in the karyosome, while the cystic cytoplasm and the chromatoid bars were strongly positive.

Deoxyribonucleic acid (DNA) was present in the nucleus in small granules arranged as a single layer beneath the nuclear membrane and as a number of small granules surrounding the karyosome. DNA was sometimes detected in small granules scattered throughout the endoplasm of amoebae and the cystic cytoplasm. The chromatoid bars gave a faint reaction. Whereas DNA was present mainly in the nucleus, ribonucleic acid (RNA) was found mostly in the cytoplasm of amoebae and cysts. However, RNA was also detected in the nucleoplasm and the nuclear membrane. The chromatoid bars contained a large amount of RNA.

The association of these nucleic acids with phosphatases in the chromatoid bars leads the authors to suggest that an active DNA–RNA turnover takes place in these structures.

R. A. Neal

BACTERIA

596. Nasal Carriage of *Staphylococcus aureus* in the General Population and its Relationship to Hospitalization and to Penicillin Therapy

P. M. ROUNTREE, B. M. FREEMAN, and R. G. H. BARBOUR. *Medical Journal of Australia* [*Med. J. Aust.*] 2, 457–460, Sept. 18, 1954. 14 refs.

An investigation was carried out among blood donors in Sydney to determine the incidence of nasal carriers of *Staphylococcus aureus* and at the same time the incidence of penicillin-resistant strains of staphylococci, the findings being compared with those obtained in a similar investigation in 1951. Nasal swabs were taken from each donor, who was also asked whether he had received penicillin during the last 5 years or had attended hospital during that period. All strains of staphylococci isolated were examined for coagulase production, and the sensitivity of coagulase-positive strains to penicillin, streptomycin, chloramphenicol, oxytetracycline, and chlortetracycline was determined by the plate disk method, these strains also being phage typed.

Of 200 donors, 98 (49%) were carriers of *Staph. aureus*, an incidence similar to that previously found in blood donors. In 13 (13·3%) of these carriers penicillin-resistant strains were found, this being an increase of 6% over the figure for 1951, the difference being regarded

as a trend rather than as a statistically significant finding. No streptomycin- or chloramphenicol-resistant strains were found. Of the 13 penicillin-resistant strains, 12 belonged to Group III and one could not be typed. The frequency distribution of the penicillin-sensitive strains in the various phage groups was similar to that found in previous investigations on healthy subjects.

Of the 200 donors, 88 had had some form of penicillin therapy; 49 of these were carriers, including 8 of the 13 from whom penicillin-resistant strains of *Staph. aureus* were isolated. Of the 47 donors who had been in hospital, 27 were carriers, penicillin-resistant strains being isolated from 4; of the 153 who had not been in hospital, 71 were carriers.

The authors consider the findings to indicate that there is " a gradually increasing incidence of penicillin-resistant staphylococci outside hospitals ". Further, the acquisition of these strains by patients while in hospital and the selection of resistant mutants during penicillin therapy probably contribute to this increasing incidence.

R. B. Lucas

597. **Bacteriophage Typing of Staphylococci. I. Technique and Patterns of Lysis. II. Epidemiologic Studies among Patients, Household Contacts, and Hospital Personnel. III. Relationship to Antibiotic Sensitivity and Resistance**

G. G. JACKSON, H. F. DOWLING, and M. H. LEPPER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 14–28; 29–40; 41–50, July, 1954. 13 figs., 31 refs.

In the first of these three papers from the University of Illinois College of Medicine, Chicago, the authors describe their technique of bacteriophage typing of 2,085 strains of staphylococci, and of preparing and propagating the phage [for details of which the original paper should be consulted]. They divided their phages into three main groups (and a number of subgroups) after the pattern of Williams and Rippon (*J. Hyg.*, 1952, **50**, 320; *Lancet*, 1953, **1**, 510), but designated I, II, and III. They found, however, that the frequency of lysis of the coagulase-positive staphylococci by the phage was less than that obtained by other workers, being 35·2% of the coagulase-positive strains examined. Only one coagulase-negative strain showed any significant degree of lysis. They also report the percentage distribution of the typed strains among the phage groups, which corresponds to that found by Williams and Rippon.

The second paper describes the application of this technique to the examination of the distribution of phage groups among patients admitted to hospital, their home contacts, and the hospital staff. Strains of the authors' Group III were found to predominate in the respiratory tract, although strains of their Group I occurred more frequently than would be expected from a random distribution; 90% of Group-I strains were lysed by Phage 52. Group-II strains were not present with any great frequency; this is in keeping with the observations of other workers that these strains occur most frequently in staphylococcal lesions requiring surgical treatment, which were not well represented in this series. An epidemiological survey showed that strains of Groups I and II were found more frequently among the patients' household contacts and of Group III among hospital personnel, while strains from the patients themselves were found in both groups of contacts. Of a number of strains from cases of staphylococcal enteritis following antibiotic therapy, 93% were found to belong to Group III or mixed and miscellaneous groups.

In their third paper the authors describe the results of correlating the phage groups of the strains with their sensitivity or resistance *in vitro* to penicillin, chlortetracycline, and erythromycin. Strains of Groups I and II had a greater percentage of penicillin-sensitive strains, and of Groups III and III-M a greater percentage of penicillin-resistant strains than had been expected. Of the typable coagulase-positive strains, 23·4% were sensitive to penicillin, while among the non-typable strains 41·3% were sensitive. Similar investigations with chlortetracycline showed a higher proportion of resistant strains in the typable than in the non-typable group (9·4% compared with 2·5%). With erythromycin Group I produced less and Group III more resistant strains than had been expected.

John M. Talbot

598. **A Simple Procedure for the Identification of the Genus *Salmonella* by Means of a Specific Bacteriophage**

W. B. CHERRY, B. R. DAVIS, P. R. EDWARDS, and R. B. HOGAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 51–55, July, 1954. 11 refs.

In this paper from the Communicable Disease Center, U.S. Public Health Service, Atlanta, Georgia, the authors describe their technique of using a bacteriophage as a diagnostic agent in the identification of organisms of the *Salmonella* group, the phage employed being that designated " O-1 " by Felix and Callow (*Brit. med. J.*, 1943, **2**, 127). This phage was found to lyse 415 (97%) of 427 strains of *Salmonella* tested, and all of 29 diphasic cultures and 6·2% of 162 monophasic cultures of Arizona paracolon bacilli, while lysing only an occasional member of other types of *Enterobacteriaceae*. The method employed is cheaper and much more rapid than the identification of *Salmonella* organisms by serological typing, and is of particular value when large numbers of cultures must be examined, the authors stating that from 200 to 400 cultures can be tested with ease by one person during a single working day.

John M. Talbot

599. **The Relationship of " Atypical " Acid-fast Bacteria to Human Disease. A Preliminary Report**

A. TIMPE and E. H. RUNYON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 202–209, Aug., 1954. 30 refs.

Acid-fast bacteria other than the known human and bovine tubercle bacilli are not infrequently isolated from patients with pulmonary disease. At the Veterans Administration Hospital, Atlanta, Georgia, a study has been made of such " atypical " bacteria which have been isolated from 88 patients known or suspected to have pulmonary tuberculosis. These organisms were

recovered from sputum, gastric washings, bronchial aspirate, pleural fluid, and lung tissue. Their cultural characteristics and pathogenicity have been studied and compared with those of known virulent and avirulent organisms.

On the basis of colonial characteristics it was possible to divide the organisms into three groups. None of the groups was pathogenic to guinea-pigs, but Groups I and III were pathogenic to mice. The organisms displaying mouse virulence were often isolated repeatedly over long periods of time from the sputum of patients with symptoms of pulmonary tuberculosis, from none of whom, however, had positive cultures of *Mycobacterium tuberculosis* ever been obtained. There were 24 of these strains altogether, 7 of them being found directly in diseased lung tissue removed at operation. When tested in mice all 24 strains caused lung lesions. On the other hand Group II contained 17 strains which were not virulent in mice and were not consistently associated with human disease. These organisms were often found in much lower concentration in the original specimens, and a high proportion of them were isolated from gastric washings. Many of the patients harbouring these atypical bacilli were also harbouring typical human tubercle bacilli as well.

The authors suggest that the atypical acid-fast bacilli in Groups I and III appear to be associated with human pulmonary disease, and that therefore such organisms should not be disregarded because they are not typical *Myco. tuberculosis*, especially if recovered from a patient with pulmonary disease. *R. F. Jennison*

SEROLOGY AND IMMUNOLOGY

600. Nonspecific Reactions with the Middlebrook–Dubos Test for Tuberculosis Antibodies

B. GERSTL, D. KIRSH, J. W. WINTER, S. B. WEINSTEIN, A. G. HOLLANDER, P. COVA, and M. BARBIERI. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 44, 443–448, Sept., 1954. 15 refs.

In experiments carried out at the Veterans Administration Hospital, Oakland, California, it was found that rabbits receiving immunizing injections of staphylococci or streptococci produced antibodies of high titre which reacted to the Middlebrook–Dubos test for tuberculosis antibodies. Rabbits receiving injections of mineral-oil adjuvants produced low-titre antibodies which reacted to the test. The specific reaction against tuberculosis antibodies was inhibited by a dilution of 10^{-6} of old tuberculin (O.T.) but the non-specific reaction was inhibited only by a dilution of 10^{-3} of the same O.T.

The sensitizing agent in tuberculin is believed to be a polysaccharide. Immune streptococcal and staphylococcal antisera absorbed with O.T.-sensitized erythrocytes retained their ability to react with the somatic polysaccharide from pneumococcus Type II and with Cx-reactive protein antiserum. At least two antibodies, therefore, are probably present in these immune antisera. In adjuvant antisera the Cx-reactive protein was removed by the same technique, suggesting that this protein is the component of the antiserum which reacts with O.T.-sensitized erythrocytes. This suggestion received support from the coincidence of the appearance of this protein and of reactivity to the Middlebrook–Dubos test in the serum of rabbits which had received an injection of an adjuvant.

Immune sera, after absorption by the homologous polysaccharide, still reacted to the Middlebrook–Dubos test and with Cx-reactive protein antiserum. After absorption of immune sera with suspensions of whole staphylococci and streptococci, the reactivity of the tuberculosis immune, streptococcal immune, and adjuvant sera to the Middlebrook–Dubos test remained unaltered; the reactivity of the staphylococcal immune serum was removed by a concentrated suspension of the homologous organisms. Reactivity with Cx-reactive protein antiserum was preserved in the tuberculosis and streptococcal immune sera. *M. Lubran*

601. The Ability of Pertussis Vaccine to Produce in Mice Specific Immunity of a Type not Associated with Antibody Production

D. G. EVANS and F. T. PERKINS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] 35, 322–330, Aug., 1954. 1 fig., 7 refs.

The authors, from the University of Manchester, describe a form of immunity which develops in mice within a few hours of the injection of a single dose of pertussis vaccine and is unrelated to any recognizable circulating antibody. A high level of specific immunity to infection is observed several days before the usual antibodies are detected. One of the vaccines used in the experiments was a bacterial extract known for its poor antibody response, and this was as effective in inducing this very early immunity as the best whole bacterial vaccine. It was found that as early as 5 hours after intraperitoneal injection into mice of a pertussis vaccine, over 30% of the animals withstood an intracerebral challenge dose of between 75 and 100 LD_{50} of the standard strain of *Haemophilus pertussis*. As the interval between immunization and intracerebral infection lengthened from 5 hours to 10 days the percentage of survivors increased from 30 to over 90. There was no evidence of any protective antibody (agglutinin or complement-fixing antibody) in the serum of the mice exhibiting this high degree of immunity. One ml. of pooled serum from mice showing good immunity to the intracerebral injection of 100 LD_{50} of *H. pertussis* failed to protect passively against infection with less than one LD_{50}.

The authors consider that this early immunity—produced after a single injection of pertussis vaccine—is different from that associated with antibody production, and suggest that it might be related to a type of " interference phenomenon ". Evidence is produced to show that the effect is associated solely with pertussis vaccine; a variety of other antigens all failed to induce immunity.

[These observations are of great interest and call for further investigation, which, the authors indicate, is proceeding.] *H. J. Bensted*

Pharmacology

602. Dose–Response Curves for the Effect of Histamine on Acid Gastric Secretion in Man

H. M. Adam, W. I. Card, M. J. Riddell, M. Roberts, J. A. Strong, and B. Woolf. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 329–334, Sept., 1954. 3 figs., 19 refs.

The secretory behaviour of the stomach in response to the prolonged intravenous infusion of histamine solutions has been studied in 3 men at the Western General Hospital (University of Edinburgh), Edinburgh. Gastric juice was collected throughout by continuous suction. The subject had no breakfast, and the basal output of acid was first studied during an hour's infusion of 0·9% saline solution. This was then replaced by a solution of histamine. The response began within a few minutes of starting the infusion, and a roughly steady rate of secretion of acid was attained during the second and third hours of the histamine infusion which was usually slightly less than the maximum rate, reached within the first 90 minutes. The solution of histamine was infused at a constant rate from a motor-driven syringe, the dosage ranging from 0 to 117 mμg. per kg. body weight per minute. In each subject the response increased with dosage of histamine, and a sigmoid curve was obtained by plotting response (average hourly rate of secretion of acid in the second and third hours less basal rate of secretion) against log. dose of histamine in mμg.per kg. per minute.

Theoretical dose–response curves representing two different theories of the mode of action of histamine were fitted to the data by the method of maximum likelihood; an equally good fit was obtained with each, so that it was impossible to rule out either of these theories. One assumed a population of secretory units each capable of an all-or-none response but differing in threshold sensitivity to histamine, the relation between sensitivity and log. dose following the normal probablity integral curve. The other assumed a population of identical secretory units each being active only in combination with a definite number of molecules of histamine, the data fitting the logistic curve. Of the 3 parameters fully specifying each curve, a vertical-scale parameter which can conveniently be taken as H, the estimate of the secretory maximum, is the easiest to interpret and is considered to be the chief, and perhaps the only, parameter necessary to define the gastric secretory response to histamine. In 2 of the subjects the estimates of H were significantly different ($34{\cdot}6 \pm 2{\cdot}5$ and $19{\cdot}1 \pm 1{\cdot}2$ m.Eq. of HCl per hour), although the rates of excretion of histamine in the urine were about the same. The difference between these values for H may represent a difference in the mass of secretory tissue in the 2 subjects. The other parameters are a location parameter which may be identified with the ED_{50} (dose eliciting half the maximum response), which depends on the sensitivity of the cells and on the rate of disappearance of histamine from the blood, about which little is yet known, and a horizontal-scale parameter which may be taken as b, the reciprocal of the standard deviation of the tolerance distribution in log.-dose units.

The desirability of allowing for the non-parietal component of the juice was investigated by means of the method proposed by Fisher and Hunt (*J. Physiol.* (*Lond.*), 1950, **111**, 138). Estimated values for the parietal secretion fitted the logistic curve reasonably well. The values for non-parietal secretion bore no relation to the log. dose of histamine. It was concluded that the procedure had no practical advantage over that using total acid output as index of response.

The threshold rates of infusion of histamine were found to be 4, 9, and 13 mμg. per kg. per minute in these 3 subjects: at these rates and up to 30 mμg. per minute increased gastric secretion was the only apparent clinical effect.

It is suggested that the dose–response curves obtained in this way may be useful in comparing the secretory responses of different stomachs or of the same stomach after various treatments.

[This is a most valuable contribution to the study of the secretory response to histamine in man. It confirms a previous estimate of the threshold rate of infusion necessary for secretion and indicates a useful method for assessing differences in secretory response in different people and before and after treatment.]

Derek R. Wood

603. Physiological and Pathological Effects of Long-term Polyvinylpyrrolidone Retention

W. A. Altemeier, L. Schiff, E. A. Gall, J. Giuseffi, D. Freiman, G. Mindrum, and H. Braunstein. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **69**, 309–314, Sept., 1954. 3 figs., 10 refs.

Polyvinylpyrrolidone, or PVP, has been found to be an effective plasma volume expander in cases of shock. Originally introduced in 1943, it was administered to approximately 300,000 German casualties on the Russian front. Of recent years considerable attention has been given to PVP as a plasma substitute suitable for stockpiling for emergency use in treating mass casualties. Its chief drawback, however, is that after intravenous infusion 35 to 49% is retained in the body indefinitely.

In this paper from the University of Cincinnati the authors describe their observations on 23 patients who had received an intravenous infusion of 1,000 ml. of 3·5% PVP 20 months previously. Serial laboratory investigations were carried out every 2 to 8 weeks, and in addition the post-mortem findings in 7 cases in which death was due to intercurrent and unrelated causes were available. No anaphylactic or toxic effects were noted immediately after the infusion or later. In none of the

cases was there enlargement of the spleen or liver, and no disturbance of blood grouping was observed. During the follow-up period there was a slight or moderate increase in the erythrocyte count, the haemoglobin level, and haematocrit reading, but the leucocyte count and the differential count were unchanged. In all cases the erythrocyte sedimentation rate increased immediately after the infusion, this persisting for 16 months in 14 cases. The only abnormalities observed in response to liver function tests were a temporary increase in the cephalin flocculation in 11 cases and, during the first 2 months, abnormal retention of "bromsulphalein" in 5 cases. After this, only sporadic increases were observed.

On examination of liver biopsy specimens it was found that after the eighth week deposits of a pale, basophilic, globular material appeared within the Kupffer cells in increasing amounts. Later specimens showed larger accumulations, which distended the phagocytes or filled the sinusoids, compressing the adjacent liver cells. There was little doubt that the substance was PVP. Material obtained at necropsy was examined by a special method of differential staining devised to show PVP by its avidity for Congo red. It was found that PVP was retained in significant amounts, and was regularly demonstrable in the spleen, lymph nodes, liver, bone marrow, and adrenal cortex, the deposits appearing in the histiocytes, which were uniformly filled with the substance. PVP was also found in the heart, lungs, arteriosclerotic plaques of the aorta, pancreas, kidney, bladder, prostate, gall-bladder, oesophagus, and thyroid gland, but not in other organs. The inconstant appearance in these non-storage organs was thought to represent a response to local injury, inflammation, or repair. Further investigations are being carried out to determine whether the prolonged retention of PVP ultimately causes sufficient deleterious effects to preclude its use as a substitute for plasma. *Robert Hodgkinson*

604. Clinical Experience with Coumarin Anticoagulants Warfarin and Warfarin Sodium

D. V. CLATANOFF, P. O. TRIGGS, and O. O. MEYER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 213–220, Aug., 1954. 4 figs., 8 refs.

"Warfarin" (3-(α-phenyl-β-acetylethyl)-4-hydroxycoumarin), like other 3-substituted-4-hydroxycoumarin compounds, produces hypoprothrombinaemia on oral or intravenous administration. When massive oral doses are given to rats its presence can be detected spectrophotometrically in the plasma within 4 hours. The plasma concentration curve is not affected by giving vitamin K_1 simultaneously, although this gives complete protection against the toxic and anticoagulant actions of warfarin. On intravenous injection the drug rapidly diffuses through the rat's body and is found in maximum concentration in the muscles, plasma, and liver 5 minutes after injection.

In therapeutic tests carried out at the University of Wisconsin Hospitals, Madison, warfarin was administered intravenously to 20 patients and orally to 16 patients, 25 of these patients having evidence of thrombo-embolic disorders. Prothrombin times were determined by the method of Quick, the control time being usually 12 seconds. The satisfactory therapeutic range was taken to be between 25 seconds (20% of normal) and 17 seconds (40% of normal). The initial dose of warfarin used was 1 mg. per kg. body weight, while subsequent dosage varied with the response. The prothrombin time was within the therapeutic range 24 hours after intravenous administration in 16 out of 20 cases, and 36 hours after in the remainder. Serial prothrombin estimations revealed a latent period of 8 to 16 hours and a maximum effect between 48 and 72 hours after intravenous administration. Of the 16 patients who received the drug orally, the prothrombin time reached the therapeutic level within 24 hours in 15, the determination being inadvertently omitted in the remaining one. Ten patients received maintenance therapy, the drug usually being given every day, every other day, or occasionally every third day in doses of 12·5 or 25 mg. according to the prothrombin time.

It is concluded that warfarin compares favourably in activity with the other coumarin anticoagulants. In regard to latent period and the time required to reach therapeutic levels it is similar to ethyl biscoumacetate ("tromexan"), but its duration of action is more prolonged, making it less difficult to maintain a stable level of hypoprothrombinaemia. The latent period and the time required to reach therapeutic levels are shorter with warfarin than "cyclocumarol" or bishydroxycoumarin, while the duration of effect is similar. There is no advantage in giving the drug intravenously unless the patient is unable to tolerate oral medication. Vitamin K_1 proved to be a very effective antidote to the induced hypoprothrombinaemia. Hypersensitivity to the drug was seen in 3 patients, one of whom was later found to have metastatic liver involvement. As with other 4-hydroxycoumarin compounds, microscopic haematuria was occasionally seen as a toxic manifestation.

Robert Hodgkinson

605. Bronchodilator Activity of Three New Drugs in Patients with Pulmonary Emphysema

A. LESLIE, D. A. DANTES, and L. ROSOVE. *Diseases of the Chest* [*Dis. Chest*] **26**, 295–305, Sept., 1954. 1 fig., 6 refs.

An investigation was undertaken at the Veterans Administration Center, Los Angeles, to evaluate the bronchodilator properties of three new drugs. These were administered intravenously to 17 patients with pulmonary disease and associated bronchospasm, and the results assessed by ventilometric measurement of vital capacity, maximum breathing capacity, volume of deep respiration, and breathing reserve. Only one of the drugs—"antrenyl" (oxyphenonium bromide; diethyl(2-hydroxyethyl)methylammonium bromide α-phenyl-*cyclo*hexane glycolate)—appeared to offer definite indications of therapeutic value, and the bronchodilator activity of this preparation was studied in greater detail. A further 45 patients, more severely incapacitated than the previous group, were treated with the drug in the form of a nebulized aerosol, 0·5 mg. of antrenyl being

diluted with 1 ml. of distilled water and delivered with oxygen at a pressure of 20 cm. of water. Benefit was observed in 38 patients.

The authors presume that, because of the drying effect of anticholinergic preparations generally, antrenyl should not be used in the treatment of bronchial asthma, but only when bronchospasm is associated with the production of much sputum. *A. W. Frankland*

606. **Depression of the Cough Reflex by Pentobarbitone and Some Opium Derivatives**

A. J. MAY and J. G. WIDDICOMBE. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] 9, 335–340, Sept., 1954. 6 figs., 15 refs.

In experiments carried out at the Nuffield Institute for Medical Research, University of Oxford, the effects of certain drugs on the cough and other respiratory reflexes and on respiration in anaesthetized cats have been observed. To elicit the cough reflex a mechanical stimulus was applied by touching the carina with a polythene catheter passed down the trachea; alternatively, addition of sulphur dioxide to the inspired air provided a chemical stimulus to cough. With the mechanical stimulus an initial expiratory effort was followed by an inspiratory gasp, whereas the chemical stimulus provoked predominantly inspiratory efforts. The drugs were given intravenously at intervals of 5 or 10 minutes, each reflex being elicited once between doses. The effect of a drug on the cough reflex was assessed in terms of the ratio of the initial expiratory or inspiratory volume after the stimulus to the average preceding tidal volume.

Morphine (5 cats) was the most active of the drugs used in abolishing the expiratory response to a mechanical stimulus. Pholcodine (7 cats) was only half as effective as morphine, but significantly (3 times) more so than codeine (11 cats). Pentobarbitone abolished this reflex only if used in doses causing profound respiratory depression or death. The inspiratory gasp after inhalation of SO_2 was most readily abolished by morphine and by pentobarbitone; pholcodine was less effective in its action on this type of response, being in fact less active than codeine. Comparison of the doses required to block the inspiratory components of both types of coughing and those required to block the expiratory component of the response to mechanical stimulation showed that whereas pentobarbitone and codeine affected the two components equally, morphine was more effective against the inspiratory responses and pholcodine more effective against the expiratory response. These quantitative differences probably explain the apparent greater efficacy of morphine against chemical and of pholcodine against mechanical stimuli.

Tidal volume and rate of respiration were depressed by morphine and by pentobarbitone, whereas codeine had a variable effect, causing respiratory depression in 6 cats and stimulation in 3, the mean result being an increase in minute volume. The action of pholcodine resembled that of codeine rather than that of morphine; neither pholcodine nor codeine affected the respiration of vagotomized cats, so that their action is probably not central. The Hering–Breuer inflation reflex was depressed by pentobarbitone but greatly enhanced by the opium derivatives, the respiratory inhibition being increased up to 10-fold. This might be due to depression of the response to hypercapnia and anoxia, but since the response to inhalation of 5% CO_2 was not greatly affected by codeine it is more probable that the enhancement of the Hering–Breuer reflex is due to increased activity of the pulmonary stretch receptors associated with the bronchoconstriction caused by these drugs.

It is considered that although a direct action of these drugs on the cough receptors cannot yet be excluded, their main effect in depressing the cough reflex is probably central—but not on the respiratory half-centres themselves, since pentobarbitone depresses respiration without blocking the cough reflex and pholcodine blocks the reflex without causing respiratory depression. Implications of the demonstration of two different types of cough reflex are discussed in relation to the possible existence of a cough centre or centres proximal to the respiratory centre. *Derek R. Wood*

607. **Contribution to the Pharmacological and Toxicological Study of Di-(terbutyl):-naphthalene Sodium Sulphonate.** (Contribution à l'étude pharmacologique et toxicologique du di-terbutyl naphtalène sulfonate sodique)

G. R. DE VLEESCHHOUWER. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] 97, 34–53, Feb. 1, 1954. 4 figs., 11 refs.

Di-(terbutyl)-naphthalene sodium sulphonate (L1633, " bécantex ") is claimed to be a good cough-depressant and is active when given by mouth. The present study was undertaken at the University of Ghent in order to investigate its pharmacological properties more fully and to test its possible toxicity, in view of its chemical nature and the possibility of its causing phenol intoxication.

Toxicity tests in guinea-pigs indicated that, except for local irritant effects and severe pain on repeated injection, the drug produced no general toxic effects when given subcutaneously in doses up to 5 mg. per kg. body weight daily for 3 weeks. In another group of 20 guinea-pigs given 10 mg. per kg. daily, 3 animals died, death being mainly due to the extension of local necrotic lesions at the site of injection. In single doses up to 100 mg. per kg. body weight the drug caused only local irritation. The minimum lethal dose was shown to be 250 mg. per kg., death occurring from cardiovascular or respiratory failure after initial ataxia and paralysis.

In anaesthetized dogs doses above 30 mg. per kg. body weight caused circulatory changes and irregularity of respiration. Carotid-sinus reflexes were unaltered after a dose of 80 mg. per kg. In dogs given a sedative dose of urethane the intravenous injection of 10 to 20 mg. of L1633 per kg. body weight abolished all coughing response to inhalation of an aerosol mist of N/2 sulphuric acid. The substance has no central depressant effect and does not, like codeine, depress the cough reflex by central action, its effect on the respiratory tract being apparently exerted entirely peripherally.

Derek R. Wood

Chemotherapy

608. **The Antibiotic Properties and Tolerance of Argicillin. Comparison with Gramicidin.** (Propriétés antibiotiques et tolérance de l'argicilline. Comparaison avec la gramicidine)

A. QUEVAUVILLER, A. DESVIGNES, and S. GARCET. *Presse médicale* [*Presse méd.*] **62**, 1268–1269, Sept. 25, 1954. 3 figs., 4 refs.

Argicillin is a new substance derived from gramicidin (tyrothricin) by treating the latter with formaldehyde. Chemically it is hydroxymethylgramicidin and occurs as a white powder which is stable to heat and slightly soluble in water. In tests carried out at the Institute of Pharmacodynamics, Paris, its bacteriostatic activity *in vitro* was shown to be equal to that of tyrothricin against pneumococci; tyrothricin was slightly more effective against streptococci and enterococci, whereas argicillin was the more active against *Neisseria catarrhalis*, *Staphylococcus aureus*, and *Gaffkya tetragena* (*Micrococcus tetragenus*). Neither drug had much action on *Bacterium coli*. When injected intravenously in propylene glycol into mice argicillin proved to be five times less toxic than tyrothricin, repeated intraperitoneal injection for 15 days producing only slight evidence of liver damage and no alteration in the erythrocyte count; tyrothricin in similar dosage caused toxic necrosis of the liver and an anaemia which was probably due to the haemolytic effect of the drug, experiments *in vitro* with rabbit erythrocytes having shown marked haemolysis. The authors conclude that argicillin may therefore be clinically useful in suitable conditions, and less likely to produce the side-reactions of tyrothricin.

Derek R. Wood

609. **The Significance of Resistance of *Mycobacterium tuberculosis* to Isoniazid**

R. N. JOHNSTON and R. W. RIDDELL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 442–452, Sept., 1954. 5 figs., 12 refs.

Bacterial susceptibility tests are usually performed at infrequent intervals on cultures of *Mycobacterium tuberculosis* obtained from various sources. In order to ascertain whether such infrequency gives an adequate picture of the incidence of bacterial susceptibility to isoniazid, tests were carried out on cultures obtained twice weekly from 31 patients at the Brompton Hospital for Diseases of the Chest, London, who were being treated with isoniazid alone or isoniazid in combination with other drugs.

It was found that the frequency of sputum examination influenced the probability of finding isoniazid-resistant strains in patients receiving this drug. Examinations made at frequent intervals showed that bacterial resistance of strains isolated from serial cultures was not necessarily a permanent phenomenon once it appeared. The isolation of a single culture resistant to 1 μg. of isoniazid per ml. should not be the sole reason for discontinuing the drug. It is argued that the isolation of a culture of *Myco. tuberculosis* growing in the presence of 5 μg. of isoniazid per ml. indicates a degree of bacterial resistance which is likely to recur later. *A. W. H. Foxell*

610. **Metabolism of Isoniazid in Man as Related to the Occurrence of Peripheral Neuritis**

H. B. HUGHES, J. P. BIEHL, A. P. JONES, and L. H. SCHMIDT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 266–273, Aug., 1954. 1 fig., 18 refs.

The relation of the metabolic fate of isoniazid to the occurrence of peripheral neuritis has been studied in a group of 17 patients treated with relatively large doses of this drug. The results have indicated the existence of three different mechanisms in the degradation of isoniazid. The first and preferred mechanism involves acetylation of the terminal nitrogen of the hydrazine moiety; the second, cleavage of the hydrazine to form *iso*nicotinic acid or a closely related derivative; and the third and most difficult to achieve, degradation to an as yet undefined moiety. The occurrence of peripheral neuropathies was closely associated with an apparent defect in the acetylation of isoniazid and the presence of the third pattern of degradation.—[Authors' summary.]

611. **The Possibility of Counteracting the Toxic Effects of Isoniazid.** (Sulla possibilità di antagonizzare gli effetti tossici dell'isoniazide (INI))

S. GARATTINI, E. MUSSINI, and R. PAOLETTI. *Giornale italiano di chemioterapia* [*G. ital. Chemioter.*] **1**, 262–269, April–June, 1954. 13 refs.

The authors have investigated in frogs, mice, rats, and guinea-pigs the possibility of neutralizing the toxic effects of isoniazid by the administration of sulphurated amino-acids. They found that methionine, cysteine, cystine, and taurine were markedly effective in this respect, not only in reducing mortality, but also in lengthening the survival time. Glutamic acid in large doses also reduced the toxicity of isoniazid, but not so markedly as the other amino-acids.

In view of the similarity of the toxic action of isoniazid to that of ammonium chloride the authors suggest that both these substances produce a fall in the level of -SH groups in the liver and that this fall is prevented by the administration of the above amino-acids or of adenosine triphosphate. The metabolism of ammonia in the liver appears to be different from that in nervous tissue, and it is suggested that isoniazid does not diminish the concentration of -SH groups in the cerebral tissues, a fact which may explain why it occasionally produces convulsions. The authors draw two conclusions: (1) that the toxicity of isoniazid is due to the excessive production of ammonia in the tissues; and (2), which may be of practical application, that greater doses of isoniazid could be used if sulphurated amino-acids were administered simultaneously. *R. F. Jennison*

Infectious Diseases

612. **Effect of Cortisone on Calcium Metabolism in Sarcoidosis with Hypercalcaemia: Possible Antagonistic Actions of Cortisone and Vitamin D**
J. ANDERSON, C. E. DENT, C. HARPER, and G. R. PHILPOT. *Lancet* [*Lancet*] **2**, 720–724, Oct. 9, 1954. 6 figs., 29 refs.

The authors, from University College Hospital, London, describe 4 cases of sarcoidosis with the rare complication of hypercalcaemia accompanied by impaired renal function, and report the results of treatment with cortisone in doses ranging from 50 to 150 mg. daily. Calcium balance studies before treatment showed that faecal calcium was less than normal, the amount of calcium excreted being 33 to 75% of the intake instead of 85 to 90%. After administration of cortisone the faecal excretion of calcium increased and the plasma calcium level fell, thus reversing the metabolic effect of calciferol.

The authors believe that the hypercalcaemia in these cases may have been due mainly to over-absorption of calcium from the intestine as the result of abnormal sensitivity to calciferol, although erosion of bone by sarcoid deposits may have been a contributory factor. They suggest that cortisone and calciferol may have antagonistic actions. Since cortisone did not depress the serum calcium level in a case of hyperparathyroidism, the authors consider that the drug should be used to distinguish this form of hypercalcaemia from that found in sarcoidosis. *D. G. Adamson*

613. **Treatment of Pertussis with Intramuscular Oxytetracycline**
B. NEWMAN, G. GAVIS, and S. WEINBERG. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 934–938, Sept., 1954. 47 refs.

This article contains a summary of the literature on the use of various antibiotics in the treatment of pertussis and includes a report on 40 patients treated by the authors at Kingston Avenue Hospital, Brooklyn, New York, with intramuscular oxytetracycline. A total of 5 mg. per kg. body weight was given daily in 2 or 3 doses for an unstated period. The diagnosis was made from the history and physical examination, and detailed records were kept of the radiographic appearances, blood count, number of paroxysms, and the occurrence of vomiting and cyanosis.

The ages of the patients ranged from 6 weeks to 6 years, 26 being in the first year of life, and the two sexes were represented equally. The average duration of symptoms on admission was 11·4 days. By the third day of treatment there was an obvious decrease in the number and severity of spasms in all cases, the temperature becoming normal usually within 24 hours. Among the less desirable effects of treatment were induration of the buttock at the site of injection in one case, unilateral myringitis developing during treatment in one case, and return of fever when treatment was stopped on the 6th day in one case, with recovery when a second course was given.

The authors recommend the intramuscular administration of oxytetracycline in pertussis on the grounds that smaller doses suffice and, since none of the drug is lost by vomiting, accuracy of dosage is assured. Moreover, the gastrointestinal side-effects seen with oral therapy are avoided. These advantages decrease the burden of management for the nursing staff to an extent which outweighs the disadvantage of giving repeated intramuscular injection. *T. Anderson*

614. **Meningococcal Infections; with Particular Reference to Fulminating Meningococcemia (Waterhouse–Friderichsen Syndrome) Treated with Cortisone and Norepinephrine**
J. W. GRIFFIN and C. W. DAESCHNER *Journal of Pediatrics* [*J. Pediat.*] **45**, 264–272, Sept, 1954. 2 figs., 29 refs.

The clinical picture in 36 cases of meningococcal disease seen at the Jefferson Davis Hospital, Houston, Texas, between January, 1952, and September, 1953, is described, and the prognosis and treatment are discussed. In 27 cases the diagnosis was confirmed bacteriologically, *Neisseria intracellularis* being cultured from blood, cerebrospinal fluid, or skin lesions. There were 2 deaths in the series, both occurring in the group of 5 patients with the Waterhouse–Friderichsen syndrome. The management of the remaining 3 cases of the Waterhouse–Friderichsen syndrome is described in some detail. In addition to sulphadiazine and penicillin, the patients received an intramuscular injection of 25 to 100 mg. of cortisone every 6 hours, and an intravenous infusion of a solution of noradrenaline (4 mg. per litre of isotonic sodium chloride), the rate of infusion being adjusted so that the amount introduced was just sufficient to maintain the blood pressure above shock level.

R. S. Illingworth

615. **Measles Meningoencephalomyelitis**
W. F. T. MCMATH. *British Medical Journal* [*Brit. med. J.*] **2**, 789–790, Oct. 2, 1954. 9 refs.

Between September, 1951, and June, 1953, 10 cases of measles meningoencephalomyelitis were seen at Neasden Hospital, London, and in this paper the aetiology, diagnosis, and treatment of this condition are discussed. The author states that the sudden onset of nervous symptoms in a patient making an apparently normal recovery from measles should suggest the possibility of meningoencephalomyelitis. Symptoms may develop during the eruptive or the early convalescent stage; in 3 cases in the present series encephalitis preceded the rash by 2 to 3 days. Its occurrence appeared to be unrelated to the severity of the primary disease. Treatment was symptomatic, and included administration of oxygen and chemotherapeutic drugs; ACTH was

tried in 2 cases, but was ineffective. One of the patients died, and in 2 there was evidence of mental deterioration.

D. Geraint James

616. **Treatment of Severe Cases of Respiratory Paralysis by the Engström Universal Respirator**

C. G. ENGSTRÖM. *British Medical Journal* [*Brit. med. J.*] 2, 666–669, Sept. 18, 1954. 4 figs., 18 refs.

An automatic respirator which was used with success in cases of respiratory paralysis admitted to hospital during recent epidemics of poliomyelitis in Denmark and Sweden is described. A cuirass or tank respirator is often unsatisfactory if there is any respiratory obstruction from secretion in the paralysed pharynx or larynx, although the effect of the "thoracic pump" on the circulation is unimpaired. Positive-pressure controlled respiration through a tracheotomy tube overcomes the former difficulty, but the positive pressure during the inspiratory phase interferes with the return of blood to the heart. The respirator described herein is so designed that active positive-pressure inspiration is obtained through a face mask or tracheal tube, while negative pressure is actively applied to the chest wall with a cuirass during the expiratory phase; thus the mean intrathoracic pressure is lower than it is in positive-pressure inflation.

In 1953 this apparatus was used in 55 cases of severe respiratory paralysis due to poliomyelitis, and although the mortality was 27% no noxious effect on the circulation was discernible.

D. D. C. Howat

617. **Positive-pressure Inflation in Respiratory Paralysis of Poliomyelitis**

L. WISLICKI. *British Medical Journal* [*Brit. med. J.*] 2, 672–674, Sept. 18, 1954. 10 refs.

The author, writing from the Rothschild Hadassah University Hospital, Jerusalem, describes 2 cases of poliomyelitis with respiratory paralysis in which positive-pressure inflation was successfully carried out by untrained personnel using only an Oxford vaporizer fitted with a Salt valve. In the first case a non-cuffed tube was passed through a tracheotomy incision and intermittent inflation successfully carried out; in the second a non-cuffed tube was introduced through the larynx, but sufficient gaseous exchange could not be achieved without using a cuffed tube. The analogy between poliomyelitic respiratory paralysis and deliberately-induced paralysis with a relaxant drug, as in anaesthesia, is stressed.

D. D. C. Howat

618. **Absence of Tonsils as a Factor in the Development of Bulbar Poliomyelitis**

G. W. ANDERSON and J. L. RONDEAU. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 155, 1123–1130, July 24, 1954. 20 refs.

The authors have endeavoured to confirm the finding previously reported by a number of authors, that among patients with poliomyelitis of all forms, those who have undergone tonsillectomy at any time previously are more likely to develop bulbar involvement than those who have not. It is reported that out of 2,881 cases of poliomyelitis reported in the State of Minnesota during the epidemic of 1946, the authors, by domiciliary visits and questioning, were able to secure adequate histories in 2,669. Information particularly regarding previous tonsillectomy and the symptoms of the attack were obtained from the mother or a near relative, and on this information alone the cases were classified as bulbar, severe spinal, mild spinal, and non-paralytic; the criteria for classification are given. Realizing that "a classification solely on the basis of informant's history leads to certain inaccuracies" the authors compared a representative sample of the cases with their hospital records and found no marked discrepancies.

Of 1,043 patients giving a history of tonsillectomy, 36·6% had had bulbar involvement, whereas of 1,626 who gave no such history, only 9·4% suffered bulbar involvement. [Among the 2,669 patients studied there was a total of 535 bulbar cases (20%)—a much higher proportion than is usually found in Great Britain.] The total number of cases in each class and the proportion of tonsillectomized patients were as follows: 535 bulbar cases (71·4%); 936 severe spinal cases (25·3%); 908 mild spinal cases (32·6%); 290 non-paralytic cases (34·8%). The higher proportion of bulbar cases among the tonsillectomized was found to obtain for all ages. The well-known higher incidence of bulbar involvement among adults was found to be a function not so much of age as of the higher percentage of tonsillectomized patients in the older age groups. With the exception of the first month after tonsillectomy, the interval between operation and the onset of poliomyelitis did not appear to affect significantly the risks of bulbar involvement, nor were sex, social status, and previous history of respiratory-tract infections (which might have been a reason for tonsillectomy) significant factors in determining bulbar involvement.

The authors reject the hypothesis of damage to the nucleus ambiguus by the cutting of nerve fibres in the tonsillar fossae, as well as that of increased permeability of the medullary capillaries as a result of tonsillectomy. They favour Southcott's suggestion (*Med. J. Aust.*, 1953, 2, 281) that "the trauma of tonsillectomy renders the motor nerves of the tonsillar region more accessible to the entry of the virus to them from the pharyngeal surface".

[Although the authors admit that there is nothing in their findings to show that the mere presence or absence of tonsillar tissue *per se* is a factor favouring bulbar paralysis, nevertheless they frequently make statements such as "the presence or absence of tonsils is the only differentiating factor" and "the absence of tonsils predisposes to bulbar involvement", when what they really mean is the operation of tonsillectomy. It is also most unfortunate that in Table 3 of their paper the columns headed "With tonsils" and "Without tonsils" have been transposed. As to the method of the study, it might well be argued that an examination of the hospital records of all the cases would have been more accurate for the purpose of classification than a verbal investigation carried out one to 3 months after the attack.]

L. J. M. Laurent

Tuberculosis

RESPIRATORY TUBERCULOSIS

619. Significance of Hemoptysis in Apparently Inactive Pulmonary Tuberculosis

R. CHARR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 479–486, Sept., 1954. 6 figs.

Out of a total of 123 patients with pulmonary tuberculosis which had been regarded as inactive for 5 to 20 years (but who were under observation at the Pennsylvania Hospital (Jefferson Medical College), Philadelphia) 21 cases of haemoptysis occurred. In 13 of these cases investigations failed to reveal the cause, and in only 3 was it due to relapse of disease. In 2 of the remaining cases it was ascribed to non-tuberculous endobronchial lesions—one an ulcer of the left main bronchus which failed to yield tubercle bacilli, the other an area of reddening of the mucosa from which repeated attacks of haemoptysis had occurred owing to the rupture of a bronchial vessel—in 2 cases the bleeding resulted from acute non-tuberculous pneumonic infections, and in one from a bronchogenic carcinoma. The author suggests that in such cases the patient should remain in bed during the course of the investigations and be allowed to return to full activity only if all examinations are negative and there is no constitutional reaction. Investigations should include examination of the sputum and bronchial secretions for tubercle bacilli and carcinoma cells, radiography, and bronchoscopy. Examination of the oesophagus may be necessary to exclude a gastro-intestinal source.

L. Capper

620. The Role of Bronchography in Pulmonary Tuberculosis

K. M. SHAW, D. M. COLLINS, and J. MACNAMARA. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 274–284, Aug., 1954. 4 figs., 7 refs.

An investigation was carried out at the London Chest Hospital to determine the usefulness, limitations, and dangers of bronchography in pulmonary tuberculosis, with special reference to its application in surgical treatment. The authors selected 100 patients, from whom bronchograms of high technical excellence (some of which are reproduced) were obtained. "Dionosil" (which is an aqueous or oily suspension of propyliodine, the N-propyl ester of 3:5-diiodo-4-pyridone-N-acetic acid) was the contrast medium in all except 3 cases in which sulphadiazine in iodized oil was used. The patients were afebrile and the disease was considered to be in a quiet phase. After premedication with "pantopon", scopolamine, and a "decicain" (amethocaine) lozenge, the larynx, cords, and trachea were anaesthetized with "xylocaine" (lignocaine) and a Jaques catheter was passed through a nostril (also previously anaesthetized). The average amount of dionosil required was 14 to 18 ml., proper distribution being obtained by posturing.

Of the 100 patients, 72 suffered no ill-effects; 22 had a transient fever of less than 100° F. (37·8° C.) and 3 had a temperature of over 100° F., but in no case was there constitutional disturbance. A transient atelectasis occurred in one case, and in two others bronchospasm with influenza-like symptoms developed. Spread of the disease was observed in only one case in the series, this being one of the cases in which sulphadiazine in iodized oil was used. All the complications occurred in patients with extensive lesions.

The bronchograms, which were interpreted on anatomical rather than on pathological grounds, showed a degree of segmental localization not obtained by other techniques. Bronchial damage indicated disease in hitherto unsuspected areas, while in other cases its absence was a useful indication of the presence of healthy segments. Altogether, new information was obtained in 77 of the cases. The value of this information to the surgeon was demonstrated in 56 cases which came to thoracotomy, particularly by confirming the presence of uninvolved segments which could be left *in situ*. The interpretation of the bronchographic appearances proved misleading in only 4 cases in the series.

[This is an excellent piece of work, the interpretation of the findings and the conclusions being supported by reproductions of the bronchograms.]

R. J. Matthews

621. The Results of Segmental Resection for Pulmonary Tuberculosis in 260 Cases. (Résultats de 260 résections segmentaires pour tuberculose pulmonaire)

J. K. KRAAN and B. VAN DIJK. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **8**, 351–358, 1954. 16 refs.

The authors consider that segmental resection has become the most frequently practised operation in the surgical treatment of pulmonary tuberculosis, its outstanding advantage being the preservation of as much functioning lung tissue as possible. The space after resection is filled by distension of the remaining segments, and thus the development of bronchiectasis is avoided. In their experience the risks of the operation are small if: (1) the tuberculosis is sufficiently localized and other segments of the lung have never been seriously involved; (2) there has been no extension of the lesion for several months; (3) the causative bacilli are sensitive to chemotherapy; and (4) there is no active tuberculous bronchitis. The main indications for the operation are caseous masses, solitary or multiple nodules, caseous bronchitis or bronchiectasis, and localized cavities. [Detailed indications are not given.]

In a series of cases treated at the Beatrix-Oord Sanatorium, Appelscha, Netherlands, all the patients had had tuberculosis for periods of months or years, had received previous medical treatment, and had either persistent

positive sputum or residual disease thought likely to relapse. The operation was performed 260 times on 243 patients between 1949 and 1953, and there were no deaths. In 26 cases complications occurred, and in 48 positive sputum persisted after operation; in most cases this responded to medical treatment, but 2 of the 48 underwent thoracoplasty and 11 required a secondary resection. As a rule early expansion of the residual lung occurred, although sometimes it took place slowly over several weeks. In 4 cases the development of a bronchial fistula necessitated complementary thoracoplasty. In 207 of the cases postoperative recovery was uneventful. After a minimum follow-up period of 6 months, 235 (96·7%) of the 243 patients were considered to be clinically cured, more than 90% of them without further treatment, and most of them have returned to work. *M. Meredith Brown*

622. **Bacterial Resistance to Isoniazid and "Marsilid" in Treatment of Pulmonary Tuberculosis**
C. M. OGILVIE. *British Medical Journal* [*Brit. med. J.*] 2, 829–833, Oct. 9, 1954. 18 refs.

The author studied the emergence of drug resistance with 4 different regimes of chemotherapy for pulmonary tuberculosis, a small "pilot" group of patients being treated at the London Hospital with each. The groups were treated as follows: (1) (10 patients) isoniazid, 300 mg. daily, and streptomycin, 1 g. twice weekly; (2) (9 patients) "marsilid" (1-*iso*nicotinyl-2-*iso*propyl hydrazine), 300 mg. daily; (3) (17 patients) marsilid, 300 mg. daily, and streptomycin, 1 g. thrice weekly; and (4) (10 patients) isoniazid, 300 mg daily, and streptomycin, 1 g. thrice weekly. Sensitivity tests were carried out on Löwenstein–Jensen slopes containing 0·2, 1, 5, and 50 μg. of isoniazid or marsilid per ml. and 3 and 30 μg. of streptomycin per ml., plain controls being used. The duration of treatment in each case was 100 days and bacterial sensitivity was tested before, after, and at monthly intervals during the course of treatment. A high degree of cross-resistance to marsilid and isoniazid was found to occur.

Streptomycin-resistant strains were not recovered in any group but a high proportion of marsilid- or isoniazid-resistant strains emerged in Groups 1, 2, and 4. No resistant strains occurred in Group 3. The difference between Groups 3 and 4 was not accounted for by difference in types of case. Of 21 patients from whom resistant organisms were recovered after treatment with isoniazid or marsilid, 9 yielded sensitive strains 4 to 12 months later. This reversion to sensitivity did not depend on the original degree of resistance nor on the regime of treatment used, although it did seem to occur more readily in 4 cases in which treatment had lasted less than 100 days. Long duration and extensive disease, presence of cavities, and previous hospital treatment all militated against reversion. The author suggests the possibility that a combined infection with sensitive and resistant organisms might occur, in which case the finding of resistant bacteria would not necessarily preclude a clinical response to chemotherapy. Reversion to sensitivity might be due to the closure or healing of resistant foci, or to the overgrowth of resistant organisms by sensitive mutants since there is some evidence that the change is a sudden one. Patients who had consistently yielded isoniazid-resistant organisms since their treatment with that drug were not improved, and some were made worse, when given a course of marsilid. The effect of isoniazid or marsilid in similar cases where reversion to sensitivity has occurred has not been studied, but in 3 such cases in which a second course of isoniazid was given combined with streptomycin, isoniazid sensitivity was maintained after 4 to 6 weeks' treatment.

L. Capper

623. **The Increasing Frequency of Isoniazid-resistance among Patients Admitted to a Sanatorium.** (Fréquence croissante des I.N.H.-résistances chez les malades arrivant en sanatorium).
L. MEYER and M. DURAND. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 740–746, 1954. 9 refs.

624. **The Course of Pulmonary Tuberculosis during Long-term Single-drug (Isoniazid) Therapy**
K. DEUSCHLE, L. ORMOND, D. ELMENDORF, C. MUSCHENHEIM, and W. MCDERMOTT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 228–257, Aug., 1954. Bibliography.

A number of workers have already found that the antituberculous activity of isoniazid alone is equal to that of several other drugs in combination, particularly streptomycin and PAS. In the work described in the present paper the authors set out to determine the duration of effectiveness of isoniazid and, incidentally, to assess the significance of isoniazid-resistant bacilli in relation to the treatment. During the period November, 1951, to August, 1952, inclusive, 47 patients with advanced pulmonary tuberculosis (44 with cavitary disease) were given isoniazid alone by mouth in a dosage of 5 mg. per kg. body weight daily. For various reasons treatment in 15 of the cases was changed, and these patients were excluded from the final assessment; the remaining 32 continued this course, supplemented only by rest in bed with or without bathroom privileges, for one year.

In 21 of these 32 patients there was substantial clinical and radiological improvement, cavity closure being observed in 12. In 6 cases radiographs indicated a worsening of the condition, but in no instance did this represent a major spread of the disease. There were no toxic manifestations in any of the cases. At the start of treatment tubercle bacilli were cultured from the sputum of 43 of the 47 patients, and in 11 of these the strains were resistant to 1 μg. of isoniazid per ml. of medium [for details of the methods used the original paper should be consulted]. Tubercle bacilli were cultured from the sputum of only 11 of the 32 patients who completed the course. Of the 11 resistant strains, 4 had become sensitive to isoniazid.

The paper includes a lengthy presentation, with reproductions of radiographs and numerous references to the literature, of the case for administration of isoniazid alone, and for a re-appraisal of the current practice of multiple-drug therapy in pulmonary tuberculosis. [In

the abstracter's view a more detailed study of a larger series of cases (which is being undertaken) would be more convincing.] *R. J. Matthews*

625. **Studies on the Use of a High Dose of Isoniazid. 1. Toxicity Studies**
J. P. BIEHL and H. J. NIMITZ. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 430–441, Sept., 1954. 2 figs., 22 refs.

The toxic effects of high doses of isoniazid were studied in 116 patients with pulmonary tuberculosis at Dunham Hospital and the General Hospital, Cincinnati. The drug was generally given in a dosage of 6 to 20 mg. per kg. body weight daily. Peripheral neuritis, which was the commonest toxic reaction, occurred in 44% of the patients. The first symptoms were usually tingling in the fingers and toes and weakness and stiffness of the joints. At this time there were no objective physical signs; if isoniazid was withdrawn the symptoms disappeared in a few weeks, but if administration was continued tenderness of the calf muscles and increasing weakness of the limbs developed. By this time exaggerated or decreased reflexes at the knee and ankle were observed and vibration sense was absent. These symptoms persisted for many months, even if isoniazid therapy was stopped altogether. There was a definite correlation between the dose given and the incidence of neuritis. The authors noted some tendency for the neuritis to appear later in patients who had not received isoniazid before and in those who were given low doses. The neuritis could be controlled by administration of pyridoxine throughout treatment with isoniazid. Cerebral symptoms were rarely seen, but one patient died after convulsive seizures.

Anorexia with nausea and vomiting was observed in 10% of the patients within a few days of the start of treatment, but these symptoms cleared up when the dose of isoniazid was reduced by one-half. Pyridoxine effectively relieved nausea in one patient but failed to do so in 2 others. Abnormalities of liver function were observed in 9 of the 17 patients on whom liver function tests were performed, but these were not persistent, being noted on more than one occasion in only 4 patients.
G. M. Little

626. **Effect of Isoniazid upon the Emotions and the Serial Electroencephalograms of Tuberculous Patients**
M. C. ADDINGTON, D. L. WINFIELD, and S. PHILLIPS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 476–482, Sept., 1954. 14 refs.

The effect of isoniazid on the emotions and the central nervous system of 52 tuberculous patients at the Veterans Administration Hospital, Memphis, Tennessee, was assessed from the results of serial electroencephalography and the responses to the Rorschach and Bender–Gestalt tests and the Depression Scale of the Minnesota Multiphasic Personality Inventory. Of the 52 patients, 4 received 150 mg. of isoniazid daily, and the remainder received 300 mg. daily. A change in the character of the electroencephalogram was observed in only 3 cases in the series—from normal to abnormal in one, from abnormal to normal in one, and progressively abnormal in one. After 8 to 10 weeks' treatment 33 of the 40 on whom psychological tests were carried out considered they were "improved" and 7 "unimproved"; in no case did the patient consider he was worse. However, the results of the tests failed to corroborate these subjective findings. Only one patient had a psychotic episode; this cleared up on withdrawal of isoniazid and did not reappear when treatment was resumed.

The authors conclude that there is little reason to withhold isoniazid because of the mental and emotional status of a tuberculous patient. *G. M. Little*

627. **Roentgenologic Changes of the Lung Associated with Isoniazid Therapy in Pulmonary Tuberculosis**
D. SALKIN and J. A. SCHWARTZ. *Diseases of the Chest* [*Dis. Chest*] **26**, 255–263, Sept., 1954. 13 refs.

The prime purpose of the investigation here reported from the Veterans Administration Hospital, San Fernando, California, was to study the effect of isoniazid on the various types of infiltration found in pulmonary tuberculosis. A total of 106 patients (average age 49) were treated with isoniazid in doses of 150 to 400 mg. daily for 3 to 15 months. The average duration of the disease was 9 years and all the patients had a positive sputum at one time or other. The pulmonary infiltrations were classified as "exudative", "exudative–productive", "productive", and "productive–fibroid".

It was found that radiological improvement occurred in 65, 37, 14, and 4% respectively of these groups, most of the improvement taking place in the first 6 months. With regard to cavities, 23% of these became smaller, but the fibroid variety was scarcely affected. In a study of bacterial resistance made with concentrations of 0·2, 1·0, and 5·0 μg. of isoniazid per ml. of Löwenstein–Jensen medium it was found that partial resistance to 5 μg. per ml. occurred in 70% of cases at 8 months. Many of the cases of the exudative type continued to improve radiologically even after the development of this resistance, however; this was considered to be due to natural factors in the patient. Although some 60% of the patients showed no radiological improvement, they did experience subjective improvement.
Paul B. Woolley

628. **The Chemotherapy of Pulmonary Tuberculosis with Pyrazinamide Used Alone and in Combination with Streptomycin, *para*-Aminosalicylic Acid, or Isoniazid**
W. S. SCHWARTZ and R. E. MOYER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 413–422, Sept., 1954. 15 refs.

The authors, from the Veterans Administration Hospital, Oteen, North Carolina, describe the results obtained with pyrazinamide, alone and in combination with streptomycin, PAS, or isoniazid, in patients with pulmonary tuberculosis who had failed to respond to streptomycin with PAS, rest in bed, collapse therapy, and surgical measures. Pyrazinamide was given alone in a dosage of 2·8 g. daily, generally for 42 days; for combined therapy the dosage was 3 g. daily of pyra-

zinamide with 1 g. of streptomycin twice weekly, or 12 g. of PAS daily, or 300 mg. of isoniazid daily.

Of 19 cases in which pyrazinamide was given alone for 6 weeks, radiographs showed that the condition was markedly or moderately improved in 7, slightly improved or unchanged in 10, and worse in 2. All patients experienced an improvement in well-being; there was a decrease in cough and sputum, fever was abolished in 3 to 4 days, and all but one gained weight. The authors state that the results were similar to those obtained in an earlier series of cases with streptomycin alone. Attempts to determine *in vitro* the susceptibility or resistance of the organisms to pyrazinamide were unsuccessful.

In 35 cases pyrazinamide was administered with PAS. Before treatment the sputum in 16 of these contained PAS-susceptible strains of tubercle bacilli; after treatment the sputum contained PAS-resistant strains in 4 cases and was negative in the remainder. The clinical results were no better than those achieved with pyrazinamide alone; the addition of PAS did not prolong the effectiveness of pyrazinamide, while the latter did not prevent the emergence of PAS-resistant strains.

Moderate or marked radiological improvement was rarely observed in the 16 patients treated with pyrazinamide and streptomycin, and the incidence of sputum conversion was unimpressive. The sputum of 3 patients who had not received streptomycin previously contained streptomycin-resistant tubercle bacilli by the fourth month, and there was no evidence that pyrazinamide prevented or delayed the emergence of streptomycin-resistant strains.

Finally, 30 patients who had previously failed to respond to other forms of chemotherapy (which did not include isoniazid) and whose sputum contained streptomycin-resistant bacilli received pyrazinamide with isoniazid. Moderate or marked radiological improvement was observed in 15 out of 29 at the end of 4 months, in 15 out of 19 at the end of 8 months, and in 6 out of 7 at the end of a year. Tubercle bacilli were cultured from the sputum in only 5 out of 29 cases at 4 months; thereafter the sputum was negative in all cases. Of the strains cultured at 4 months, 3 were sensitive to less than 0·2 μg. of isoniazid per ml. and 2 were resistant to 5 μg. of isoniazid per ml. A few patients complained of joint pains, but other toxic symptoms were rare.

G. M. Little

629. **The Treatment of Tuberculous Sero-fibrinous Pleurisy with ACTH.** (Le traitement des pleurésies séro-fibrineuses tuberculeuses par l'A.C.T.H.)
C. Sors and Y. Trocmé. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 167–178, 1954. 14 refs.

The authors report 7 cases of tuberculous pleural effusion treated with ACTH (corticotrophin) at the Hôpital Laënnec, Paris. Detailed case histories are given. In 4 cases the effusion was acute and of short duration, in 2 it was subacute or chronic, and in one it developed after the induction of pneumothorax.

ACTH was given slowly over 8½ hours daily as an intravenous infusion in 250 ml. of glucose-saline for periods up to 14 days, along with 1 g. of streptomycin, and in some cases 250 mg. of isoniazid. The dose of ACTH in the earlier cases was 20 mg. daily, but experience showed that this could be reduced to 10 mg. daily. The authors emphasize the importance of slow administration, stating that the slower the infusion, the greater the effect of ACTH and the smaller the dose required.

The results were dramatic, ACTH producing rapid absorption of the effusion and return of the temperature to normal levels. No serious side-effects were observed.

T. M. Pollock

630. **Artificial Pneumothorax in Relation to the Effects of Antituberculotic Agents.** (De nya tuberkulosmedlens inverkan på pneumothoraxbehandlingen)
A. G. Birath and K. Heijbel. *Nordisk Medicin* [*Nord. Med.*] **51**, 639–642, 1954. 3 figs., 2 refs.

EXTRA-RESPIRATORY TUBERCULOSIS

631. **Streptomycin and Isoniazid in Acute Miliary Tuberculosis**
J. H. Lawson, A. W. Lees, G. W. Allan, and P. McKenzie. *British Medical Journal* [*Brit. med. J.*] **2**, 840–842, Oct. 9, 1954. 10 refs.

In this paper from Ruchill and Belvidere Hospitals, Glasgow, the authors compare the efficacy of isoniazid with that of streptomycin in the treatment of miliary tuberculosis. A first group of 24 patients (Series A) were treated with streptomycin between August, 1948, and June, 1951. Up to the end of 1950 adults were given 2 g. of streptomycin and, with 3 exceptions, 15 g. of sodium PAS daily, while children under 15 were given 44 mg. of streptomycin and 0·25 g. of PAS per kg. body weight daily. After 1950 the dosage of streptomycin for adults was 1 g. daily. The duration of treatment was 4 or more months. A second group of 12 patients (Series B) were treated between April, 1952, and February, 1953, with isoniazid in a dosage of 6 or 8 mg. per kg. daily, alone or combined with streptomycin or PAS or both in varying doses. The duration of treatment was 14 to 28 weeks. The diagnosis was confirmed bacteriologically or by the finding of choroidal tubercles in 20 of the 24 cases in Series A, and in all the cases in Series B.

In Series A 6 patients died, 5 of them being under 3 years of age. Tuberculous meningitis developed in 8 cases during treatment, and accounted for 3 deaths. Other complications included fulminating pulmonary infections, peritonitis, renal tuberculosis, and abscess of the chest wall. Radiological clearing of the lungs took an average of 20·3 weeks and was uninfluenced by the occurrence of meningitis. In Series B, in which none of the patients was under the age of 3, there were no fatalities and no complications during an observation period of at least a year. The average time taken for radiological clearing was 19 weeks. The authors add further cases, in one of which a child aged 9 months developed meningitis 6 weeks after commencement of therapy. They point out that isoniazid passes in high

concentration into the cerebrospinal fluid and penetrates the cell membrane of histiocytes. They conclude that it tends to prevent the development of tuberculous meningitis. *L. Capper*

632. **The Combined Treatment of Tuberculous Meningitis in Infancy with Streptomycin and Isoniazid.** (L'associazione streptomicino-isoniazidica nel trattamento della meningite tubercolare nell'infanzia)
U. MONACO, F. RUGGIERI, C. CAIONE, and G. VOLTERRA. *Annali dell'Istituto "Carlo Forlanini"* [*Ann. Ist. "Carlo Forlanini"*] **14**, 293–304, 1954. 17 refs.

Since the prognosis for life in tuberculous meningitis has become so greatly improved, the main effort must now be directed to the reduction of the incidence of sequelae, such as blindness and deafness, and the development of means of preventing the emergence of resistance of the organism to streptomycin and of increasing its effect. The authors describe 8 cases in children of 11 months to 12 years treated at the Forlanini Institute in Rome according to a schedule whose main features were: (1) use of the smallest effective dose of streptomycin; (2) daily administration until the cerebrospinal fluid is definitely returning to normal, then a gradual reduction of the dose; (3) combined systemic and intrathecal streptomycin therapy, using streptomycin and calcium chloride intrathecally, and dihydrostreptomycin sulphate systemically; and (4) additional treatment with PAS in certain cases and vitamins A and D in all cases. In addition to this standard schedule isoniazid was given by mouth in doses varying from 5 to 10 mg. per kg. body weight according to age, and intrathecally in doses of 0·5 mg. per kg. daily, being given in the same syringe with the streptomycin.

The results were very good, a relapse occurring in only one child following an attack of measles, with ultimate recovery. Three of the children had miliary tuberculosis. The most important advantages of combining isoniazid with streptomycin were the reduction in the total dosage of streptomycin needed, the more rapid return to normal of the cerebrospinal fluid, and the early increase in weight of the patients. The fact that the total treatment time can be reduced should also lessen the dangers of toxic effects of the drugs. There were only two instances of possible intolerance to isoniazid: in one case excessive sleepiness was relieved when the drug was stopped, although when the drug was reintroduced the somnolence did not return; and in the other case blood-staining of the spinal fluid ceased when administration of the drug was stopped, but when it was begun again the blood did not reappear.

J. G. Jamieson

633. **Mental Disturbances in Tuberculous Meningitis**
M. WILLIAMS and H. V. SMITH. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 173–182, Aug., 1954. 33 refs.

Cases of tuberculous meningitis provide an opportunity for observing the pattern of recovery from organic confusional states. For a study along these lines at the Radcliffe Infirmary, Oxford, patients (mostly adults) were selected who, though drowsy and irrational, were yet alert enough to answer questions and to permit of some form of psychological assessment. Tests were selected from the Wechsler, Terman–Merrill, and Babcock scales. The findings of the study are as follows.

In the prodromal phase of tuberculous meningitis mental changes are often so subtle that their existence is appreciated only in retrospect; slight clouding of awareness is frequent and contrasts with the apprehension of early poliomyelitis. There follows a "confusional state" with irrational speech and disorientation for space and time. This again is succeeded by an "amnesic state", which corresponds to the period of severe illness. At this stage, even though the patient appears alert, there is a severe retention defect, though remote memory is adequate; the symptoms are those of a "chronic organic confusional state". Finally there is the "post-recovery state", in which recovery is complete except for a sustained and absolute amnesia for the period of the illness. Intrathecal injection of tuberculin coincided with exacerbation of the mental symptoms in cases so treated.

The pattern of the mental illness in tuberculous meningitis is regarded as characteristic and approaching most closely to that of Wernicke's encephalopathy, the pathological changes being found mainly in the base of the brain, including the hypothalamus, in both conditions. However, that this localization is related to the pattern of the mental changes is regarded as no more than suggestive. *L. G. Kiloh*

634. **Antibiotic Therapy of Urinary Tuberculosis: an Interval Report of Six Years' Experience**
R. M. NESBIT and C. C. MACKINNEY. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 296–303, Sept., 1954. 2 figs.

Two years ago the authors (*J. Urol.*, 1952, **68**, 394; *Abstracts of World Medicine*, 1952, **11**, 396) reviewed 64 cases of urogenital tuberculosis given streptomycin therapy at the University of Michigan Hospital, Ann Arbor. They now present a follow-up study of the original group together with details of 26 additional cases treated since that time. Of the total of 90 patients (57 males and 33 females), 42 were suffering from unilateral renal disease, 30 had bilateral lesions, and the remaining 18 had residual cystitis following previous nephrectomy or in conjunction with genital tuberculosis. The dosage of streptomycin was 1 to 2 g. daily for 40 to 120 days (or dihydrostreptomycin, 2 g. daily up to 90 days). Patients were followed up for periods varying from 6 weeks to 6 years.

A significant feature of the investigation was the comparative failure of medical treatment alone to secure urinary conversion in patients with unilateral infection as opposed to those with bilateral lesions. Conversion of urine to negative was secured in 65 of the 90 patients (in 55 after one course of treatment). A comparison of streptomycin with dihydrostreptomycin treatment indicated that, although with the former toxic manifestations were commoner, it had the advantage of producing no apparent damage to the auditory branch of the eighth cranial nerve. *J. D. Fergusson*

Venereal Diseases

635. **Chemotherapy of Chancroid. Clinical Observations in Eighty-seven Cases**
H. E. MENDELL, D. L. FOXWORTHY, and C. G. WORNAS. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 483–486, Sept., 1954. 6 refs.

A comparative study of the therapeutic efficacy of sulphadiazine, streptomycin, chlortetracycline (aureomycin), and oxytetracycline ("terramycin") was made in the treatment of 87 cases of chancroid occurring in U.S. Air Force personnel on Okinawa. In 72% of the cases the Ducrey bacillus was isolated; all cases were followed up for 2 months after completion of therapy. The authors point out that the diagnosis of chancroid must be made cautiously in view of the many non-chancroidal lesions involving the penis. In their view the specificity of smear examination and skin tests leaves much to be desired, and they have found the clinical characteristics of the lesion and the response to conservative therapy with potassium permanganate far more reliable. The following treatment schedules were employed: (1) streptomycin, 1 g. intramuscularly daily for 7 days (22 cases); (2) sulphadiazine, 1 g. 4 times a day for 7 days (13 cases); (3) streptomycin, as above for 5 days, followed by sulphadiazine for a further 5 days (12 cases); (4) aureomycin, 250 mg. 4 times a day for 4 days (20 cases); and (5) oxytetracycline, 250 mg. 4 times a day for 4 days (20 cases).

Results showed that all four substances were equally effective in the chemotherapy of chancroid in the dosages indicated. Sulphadiazine and streptomycin in combination appeared to exert some synergistic effect and shortened the healing period of the ulcers. Since neither of these drugs has any effect on *Treponema pallidum* they are to be preferred when a syphilitic infection has not been ruled out, in order not to mask the presence of syphilis. *Neville Mascall*

636. **Erythromycin in Non-specific Urethritis**
R. R. WILLCOX. *Lancet* [*Lancet*] **2**, 684–685, Oct. 2, 1954. 8 refs.

The antibiotic erythromycin (prepared from *Streptomyces erythreus*) has given varying results in the treatment of gonorrhoea and granuloma inguinale and it also shows some potency against syphilis, but none against lymphogranuloma venereum. Pleuropneumonia-like organisms, which have often been incriminated in non-specific urethritis, are highly resistant to erythromycin; a number of workers, however, have recently tended to discount the role of these organisms in the causation of urethritis.

At St. Mary's Hospital, London, the author has treated 25 men with previously untreated non-specific urethritis with a deliberately low dose of erythromycin (100 mg. four times daily for 6 days, a total dose of 2·4 g.). In the majority of cases the urethral discharge promptly disappeared, but of 21 cases followed up, 7 (33·3%) required re-treatment, most of these being patients whose discharge had been present for 9 days or more. Mildly toxic effects of the drug were shown by looseness of the bowels in most patients, with frank diarrhoea in 3 cases, while headache, pain round the heart, and heartburn were also noted.

The author regards erythromycin as clearly beneficial in the treatment of non-specific urethritis, and deduces that such action is an added argument against pleuropneumonia-like organisms being a cause of the disease.

[So many agents have been shown to cause non-specific urethritis, and such a variety of treatments has been advocated in the past few years, that it is too early to acclaim erythromycin as other than a possibly useful adjunct to the pharmacopoeia. The number of cases here reported is too small to carry conviction, and the failure rate of 33·3% does not compare favourably with the results obtained with oxytetracycline, as described by the author in a previous communication (*Brit. J. vener. Dis.*, 1953, **29**, 225).] *Douglas J. Campbell*

SYPHILIS

637. **A Clinical and Statistical Review of Late and Unsuspected Syphilis among Patients Admitted to a Medical Unit in a Five-year Period (1948–1952).** (Rilievi clinico-statistici e terapeutici sulla sifilide tardiva ed ignorata tra i degenti accolti in cinque anni (1948–1952) in un reparto di medicina)
G. C. RICCI. *Clinica Terapeutica* [*Clin. terap.* (*Roma*)] **7**, 91–122, Aug., 1954. Bibliography.

From the Ospedali Riuniti, Leghorn, the author presents a statistical analysis of 136 cases of late or unsuspected syphilis detected between 1948 and 1952 among a total of 3,873 patients admitted to hospital in the 5 years; the annual incidence, the sex incidence, and the clinical presentation (whether cardiovascular, nervous, or other) are statistically discussed and presented in tables, while the age on diagnosis and the social status of the patients are also considered. In the male, syphilis is more likely to affect the cardiovascular and respiratory systems, the gastrointestinal tract, and the central nervous system; in the female, the biliary apparatus, the kidneys, and the peripheral nervous system are mainly affected. The author regards it as probable that the number of unknown marital infections is more than twice the number of the known marital infections.

The relation between the serum and the cerebrospinal fluid (C.S.F.) reactions to various tests for syphilis is considered in detail for four clinical groups—cardiovascular, nervous, a mixture of these two, and a miscel-

laneous group. Of the 136 patients, 86 were seropositive and 36 C.S.F.-positive; in only 11 cases did both the serum and C.S.F. give a positive reaction. The usefulness of the flocculation reaction in recognizing latent and late stages of the disease is confirmed.

It has been the author's experience that in cases with a persistent negative serological result but a positive clinical history a detailed clinical examination of the patient, especially a neuro-psychiatric examination, will often reveal positive signs.

In respect of treatment, most stress is laid on penicillin. Anaphylactic reactions due to penicillin may resemble Herxheimer reactions, but the author believes that the former occur more frequently in cardiovascular cases, whereas the Herxheimer reaction is more common in neurosyphilis. It is suggested that the Wassermann test should be performed as a routine on all patients admitted to hospital. *Ferdinand Hillman*

638. **Comparison of Spinal Fluid Findings among Syphilitic and Nonsyphilitic Individuals**

J. C. CUTLER, T. J. BAUER, E. V. PRICE, and B. H. SCHWIMMER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 447–458, Sept., 1954. 3 figs., 9 refs.

Cerebrospinal fluid obtained at the Chicago Intensive Treatment Center from 346 normal subjects, 293 patients with primary syphilis, and 477 patients with secondary syphilis were examined by the authors, the Kahn test, a cell count, and an estimation of the protein content by the modified Denis–Ayer method being carried out at the Venereal Diseases Research Laboratory, Staten Island, New York. In a second series the Kolmer complement-fixation test and the Eagle flocculation test were performed in place of the Kahn test on specimens of fluid obtained at the U.S. Public Health Services Hospital, Staten Island, from 215 normal subjects, 210 patients with primary syphilis, and 83 patients with secondary syphilis. In both series the patients were untreated at the time of examination.

In the Chicago series none of the specimens from cases of primary syphilis reacted with the Kahn test, while 10 (2%) of the secondary cases did so. In the Staten Island series 8 patients with primary syphilis (3·7%) and 24 with secondary syphilis (22·4%) gave a positive reaction with the Kolmer test. These differences were possibly due to differences in race and sex distribution between the two series and to differences in the sensitivity of the serological tests used.

In the Chicago series no differences were found in the cell count between normal subjects and patients with primary and secondary syphilis where the serological reactions were negative in the spinal fluid. Of the normal subjects the cell count was greater than 10 per c.mm. in 2·3%, whereas in the Staten Island series only one (0·5%) had a count above this level. Where the serological reactions were positive in the spinal fluid the corresponding figures were 75 and 21·9% at the two centres respectively.

In the Chicago series a protein concentration of more than 40 mg. per 100 ml. was found in 15·1% of specimens from normal subjects, in 17·4% of those from cases of primary syphilis, and in 11·5% of those from cases of secondary syphilis where the serological reactions were negative in the spinal fluid. The corresponding figures for the Staten Island series were 35·3, 13·3, and 9% respectively. The authors consider that in the absence of positive serological reactions in the spinal fluid, the total protein content alone, as measured by the Denis–Ayer method, is of little significance in indicating involvement of the central nervous system in early syphilis. Some patients who had shown high protein levels were re-examined a year after presumably successful treatment, and the level was maintained in 31 out of 45 patients. The authors suggest that this may be normal for some individuals.

[The " normal " subjects with cell counts and protein levels outside the accepted normal range were not, apparently, investigated further to exclude possible causes for these findings. The paper contains a mass of data in tabular form which cannot be compressed into an abstract, but which merits attention by those called upon to interpret spinal-fluid findings in early syphilis.] *A. E. Wilkinson*

639. **Concentration of the Cell Suspension in the Wassermann Test**

P. N. COLEMAN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 141–143, Sept., 1954. 2 figs., 9 refs.

In various well-established techniques for performing the Wassermann test considerable differences exist in the concentration of the cell suspension used and also in the periods recommended for haemolysis, yet all the methods give reliable results. The author has studied the effects of variations in these factors in the technique of his choice (that of Fairbrother and Maddocks) and found that wide variations produced relatively small effects upon the test.

The range of reagin content covered by the change from the negative reaction to the complete inhibition of haemolysis was found to increase with the cell concentration. If only one diagnostic tube was allowed for each serum test more information was obtained concerning the reagin content by using a strong cell suspension, provided that tests were read after sedimentation of the cells; there was no serious loss of sensitivity under these conditions. If it was desired to read the tests on the day they were performed it was found more satisfactory to increase the number of tubes allocated to an individual sample of serum and to use weak cell suspensions. In his experiments with sera of low reagin content the author succeeded in producing slight but quite definite inhibition of haemolysis with four different cell concentrations, but the relative degree of inhibition was greatest with the weakest cell suspension. The sharper change from a negative to a positive result seen in titration carried out with a weak cell suspension thus gave a more sensitive test. The results of experiments in which the period allowed for haemolysis was varied indicated that a long period was to be preferred. For example, if the tests were read after one hour instead of

15 or 30 minutes, haemolysis was virtually complete and the precise time of reading was not critical. The results both of the test proper and of the complement titration were found to be essentially the same whether the reading was taken at one hour or after overnight sedimentation of the cells. *A. J. King*

640. **The Problem of the Reaction between Antibody and Complement in the Wassermann Reaction Carried Out with Cardiolipin.** (Zur Frage des Bindungsverhältnisses Antikörper:Komplement bei der mit Cardiolipin ausgeführten WaR)
H. RUGE. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **140**, 163–168, 1954. 3 figs., 7 refs.

641. **The Reproducibility of Results of the TPI Test**
R. A. BOAK, J. N. MILLER, and C. M. CARPENTER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 434–436, Sept., 1954. 5 refs.

Although in some hands the *Treponema pallidum* immobilization test has failed to give consistent results on repetition in a high proportion of cases, the results in 97.4% of 874 specimens tested and retested by the authors were in complete agreement. Though no certain explanation can be given for the few disagreements, the possibility that many patients with no history of treatment for syphilis may nevertheless have received antibiotics for other diseases cannot be eliminated. The necessity for extreme care in cleansing the glassware used in the test is emphasized. *G. L. M. McElligott*

642. **Treponemal Immobilization and Standard Test Reactions in Suspected Biologic False Positive Sera**
A. H. WHEELER, K. VAN GOOR, and A. C. CURTIS. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 437–446, Sept., 1954. 17 refs.

The treponemal immobilization (T.P.I.) test has been carried out at the University of Michigan Medical School on 733 sera from patients in whom the standard tests for syphilis (S.T.S.) had been found positive at other laboratories. The T.P.I. test gave positive results in 370 cases, negative in 338, and doubtful in 25.

A tentative clinical diagnosis of syphilis had been made in 116 cases, and the T.P.I. reaction was positive in 81 of these, while of 256 patients who were thought to be non-syphilitic but had given a non-specific reaction to the S.T.S., the T.P.I. reaction was positive in 92. In 70 of these patients the history of non-specific reaction was of long duration; in 34 of the 70 in whom a suspected predisposing factor, such as lupus erythematosus or malaria, was present the T.P.I. reaction was negative; of 36 in whom no such cause was evident, however, it was negative in only 15. The presumed non-specific reaction was thought to be of the acute type in 186 patients; these included 42 patients with upper respiratory tract infections, in 33 of whom the T.P.I. reaction was negative, and 11 patients in whom the reaction had followed immunization [agent not stated], in 9 of whom the T.P.I. reaction was negative, as it was in 29 out of 39 sera from pregnant women. [This is a considerably higher incidence than other workers have found in pregnancy sera.]

An estimate of the reproducibility of the result of the T.P.I. test was made from the results of examinations of second specimens of serum from 42 patients. Identical results were obtained in 33 cases, there were minor discrepancies in 7, and in 2 cases in which the result was initially positive subsequent tests gave negative results. More than one test was made on the same specimen of serum in 195 cases, identical results being obtained in 154; in 8 an initial doubtful result was found to be definitely positive or negative on re-testing, and one serum which originally gave a positive reaction was found negative at the second test; 32 sera were either anticomplementary or toxic when first examined. The authors conclude that the T.P.I. test gives satisfactory reproducibility of results. *A. E. Wilkinson*

643. **Serology of Syphilis Based on Recent Observations**
R. L. KAHN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 124–140, Sept., 1954. 7 figs., 36 refs.

From his wide experience at the University of Michigan Medical School and the associated serology laboratory at University Hospital, Ann Arbor, the author answers two basic questions: (1) How is it possible for serum reactions employing lipid antigens, apparently unrelated to the *Treponema pallidum*, to behave as though they were specifically associated with syphilis, as shown by the remarkable parallel between serological and clinical findings? (2) How can the same serum reactions behave as though totally unrelated to syphilis, as shown by the false positive reactions noted in such a wide variety of non-syphilitic conditions?

When the Kahn precipitation test was first described it was thought that the reaction between lipid antigen and serum was limited to syphilis. Recently, however, it has been shown that the same lipid antigens which generally give specific results in serodiagnostic techniques for syphilis may in special non-serodiagnostic techniques give positive reactions in nearly 100% of normal individuals. This finding has led to the standardization of a universal serological reaction in which the Kahn antigen is used. Whereas in the Kahn quantitative technique serial serum dilutions are prepared with 0·9% sodium chloride solution, in the universal technique the serial serum dilutions are prepared with seven different strengths of sodium chloride solution ranging from 0·15 to 2·1%. The test is fully explained and a number of graphs are presented to show typical reactions in health, syphilis, lepromatous leprosy, malaria, and tuberculosis. Syphilis and the three diseases yaws, pinta, and bejel all give a similar reaction which is distinctive at the saline dilution of 0·9%, whereas the other conditions studied give more distinct reactions in the other dilutions; occasionally, however, they " spill over " into the serodiagnostic zone of syphilis tests (0·9% solution), with the resulting conflicting reports.

[This paper should be read in full by clinicians in order to appreciate the author's complex arguments; it should

be studied by serologists who are experienced in performing serological tests since they may find the universal technique helpful in detecting false positive reactions.]

Douglas J. Campbell

644. **Studies on the Treponemal Immobilization Test**
A. E. WILKINSON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 144–155, Sept., 1954. 1 fig., 27 refs.

The author's experience of the treponemal immobilization (T.P.I.) test at the Venereal Disease Reference Laboratory (Medical Research Council) and the London Hospital are here discussed in detail. The sera examined came from two sources: (1) 685 sera from syphilitic and presumed non-syphilitic patients at the London Hospital; and (2) 404 sera referred to the V.D. Reference Laboratory, largely because of anomalous serological reactions or discrepancies between clinical and serological findings.

It is concluded that in early symptomatic syphilis the T.P.I. test offers no advantages over existing diagnostic methods, while in late seropositive symptomatic syphilis the T.P.I. test does not add to the information already available. On the other hand it is of great value in the diagnosis or exclusion of suspected latent syphilis. If the T.P.I. reaction is repeatedly negative in cases giving positive serological reactions, the latter should be strongly suspected of being non-specific in nature. In the presence of signs or symptoms thought to be due to late syphilis and of negative serological reactions a positive T.P.I. reaction suggests a syphilitic aetiology. Very rarely the T.P.I. reaction may also be negative in late syphilis; of 85 sera from such cases, 11 gave a negative or doubtful result—but 10 of these sera were from treated cases. Thus it appears that the untreated patient with signs suggestive of late syphilis but whose T.P.I. reaction is negative is probably not suffering from syphilis. An interesting type needing further evaluation is the patient with early syphilis whose T.P.I. reaction remains persistently positive after treatment and in whom the serological reactions on serum and spinal fluid are negative. Whether the positive T.P.I. reaction in such patients is an ominous sign is not yet known. Specific as the T.P.I. test is, it cannot distinguish between syphilis and the other treponematoses.

G. W. Csonka

645. **Suitability of Heparinized Plasma and Deheparinized Serum in Serodiagnostic Tests for Syphilis**
C. R. REIN, S. SCHWARTZ, and L. C. KELCEC. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 405–407, Sept., 1954. 3 refs.

The purpose of this study reported from the New York University Hospital was to determine the suitability of heparinized human plasma for examination by the standard serological tests for syphilis. The heparinized specimens were converted to serum by adding 0·1 ml. (2·5 mg.) of protamine sulphate to each millilitre of plasma, the tubes then being inverted several times, a clot developing within 10 minutes. It is stated that although the serological activity of serum so prepared from heparinized plasma is apparently not impaired, microflocculation tests may be interfered with by a precipitate which appears on heating and which needs prolonged centrifugation for its complete removal; it was also noted that turbid reactions are obtained in complement-fixation tests. Heparinized plasma is thus less satisfactory than serum for serological testing.

G. L. M. McElligott

646. **Painful Aortitis.** (Des aortites douloureuses)
C. ROUBIER. *Journal de médecine de Lyon* [*J. Méd. Lyon*] **35**, 741–756, Oct. 5, 1954. 7 refs.

About one-third of all cases of syphilitic aortitis are reported to be accompanied by pain of an anginal type, this being usually attributed to fibrotic obliteration of the coronary orifices. Coronary arterial affection, however, does not explain all the cases and the author discusses this problem with special reference to 30 cases of syphilitic aortitis seen by him at Lyons since 1928 in which a detailed histological examination of the heart and great vessels was carried out. The clinical, post-mortem, and histological findings in each case are briefly detailed.

In 13 cases (6 male and 7 female) pain was present during the course of the illness, but was absent throughout in 17 cases (12 male and 5 female); the age range (42 to 72 years) was approximately the same in the two groups. A fatal termination supervened somewhat earlier in cases in which there was pain, treatment (in the pre-penicillin era) with mercury and bismuth having little effect on the course. In general, pain when it occurred was the presenting symptom and usually persisted until death. In a few cases, however, there was a gradual diminution in the frequency and intensity of the pain during the course of the disease. Two types of pain are described: (1) the classic angina occurring on effort, with typical radiation and relieved by trinitrin; and (2) an atypical anginal pain, usually more severe than (1), often abdominal in site and radiating to the scapulae but never to the arms, occurring at rest, and not relieved by trinitrin.

The pathological changes in these cases are described and their role in the causation of pain discussed. Thus it was found that obliteration of the coronary ostia occurred in 13 cases, among which, however, only 7 patients complained of pain, 2 of these having typical angina and 5 the atypical type of pain. Lesions of the coronary arteries themselves, as well as cardiac lesions and obliteration of the origin of the intercostal arteries, were similarly inconstant findings. As to the role of lesions of the aorta itself, it was observed that where painful aortitis occurred there was an intense local inflammatory reaction, with a marked periaortitis involving the periaortic nervous plexus. In contrast, in the painless group aortic lesions were confined to the media or made only slight encroachment on the adventitia. From this the author, although not denying the importance of involvement of the coronary arteries in producing pain in aortitis, concludes that the existence of an inflammatory periaortitis must nevertheless be regarded as a causal factor in some cases.

Benjamin Schwartz

Tropical Medicine

647. **Hepatic Fibrosis or Cirrhosis in Children in Djakarta.** [In English]
LIE KIAN JOE and S. TJOKRONEGORO. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop.*] **6**, 193–207, Sept., 1954. 6 figs., 11 refs.

The authors have studied the relationship between hepatic cirrhosis and malnutrition in children at the Central Hospital, Djakarta, Indonesia, liver biopsy specimens from 104 children suffering from malnutrition and 57 children without obvious signs of malnutrition being examined histologically. In the malnourished group fatty infiltration was noted in 76 out of 80 cases in which liver biopsy was performed within one week of admission. Slight fibrosis was present in 48 of the 104 specimens. Serial biopsies in 22 cases during convalescence or relapse did not reveal any definite increase in fibrous tissue. There was moderate or marked fibrosis in 16 cases, in 5 of which there was also evidence of hepatitis, consisting in degenerative changes in the parenchymal cells and infiltration with mononuclear and other cells.

Fatty infiltration was observed in 26 of the 57 children without obvious clinical signs of malnutrition. It was often slight and sometimes there were only a few small fat vacuoles in each lobule; severe fatty infiltration was not observed in any of these cases. Fibrosis of some degree was present in 28 cases; this was moderate or severe in 11, in 7 of which there was also hepatitis with clinical signs of viral hepatitis. The fibrous tissue had penetrated between the cells in some instances; this was not observed in the malnourished group. In one of the patients without obvious signs of malnutrition post-necrotic scarring was noted.

The authors do not consider that malnutrition alone leads to hepatic cirrhosis. Cirrhosis is primarily attributable to viral hepatitis, but the high incidence in children in tropical countries is determined by the prevailing malnutrition. *William Hughes*

648. **Endophlebitis Hepatica Obliterans Resulting in Juvenile Cirrhosis of the Liver.** (Endophlebitis obliterans hepatica en de daardoor veroorzaakte juveniele levercirrhose)
G. BRAS, D. B. JELLIFFE, and K. L. STUART. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 2341–2349, Aug. 21, 1954. 6 figs., 34 refs.

Further to their previous report (*Docum. Med. geogr. trop.* (*Amst.*), 1954, **6**, 43; *Abstracts of World Medicine*, 1954, **16**, 275) the authors now present a detailed clinical and histological study of 12 of the cases there described to illustrate a juvenile form of hepatic cirrhosis which occurs in Jamaican children, not typically among the poorest classes or accompanied by the more extreme degrees of malnutrition associated with kwashiorkor. The disease is analogous to the infantile cirrhosis seen in India and elsewhere. The initial condition may be acute and rapidly fatal, other cases may progress to recovery in a period of weeks or months, while in a few it may result in irreversible cirrhosis. Whether the diet is rich or poor in protein is apparently unimportant.

The essential histological lesion, observed in numerous biopsy and post-mortem examinations [and here illustrated in excellent reproductions of photomicrographs], is an endophlebitis obliterans of the hepatic central and sublobular veins which may extend to the whole hepatic network, leading to stasis, sinusoid dilatation, centrilobular necrosis, and eventually fibrosis. The portal tissue is not generally involved. The various causes that have been advanced to explain endophlebitis obliterans hepatica as an independent entity (Chiari's syndrome) are discussed in relation to the Jamaican variety. It is thought that a specific factor may be responsible, and in this connexion attention is drawn to the prevalent use in Jamaica of "bush-teas", for the preparation of which some 200 plants are used; these, perhaps significantly, include species of *Senecio*, the alkaloids of which have been used experimentally for the production of hepatic endophlebitis. *R. Crawford*

INFECTIOUS DISEASES

649. **Distribution of Microfilariae of *O. volvulus* in the Skin. Its Relation to the Skin Changes and to Eye Lesions and Blindness**
W. E. KERSHAW, B. O. L. DUKE, and F. H. BUDDEN. *British Medical Journal* [*Brit. med. J.*] **2**, 724–729, Sept. 25, 1954. 2 figs., 3 refs.

The concentration and distribution of the microfilariae of *Onchocerca volvulus* in the skin and their relationship to skin changes and to eye lesions and blindness in infected subjects were studied among the population of the British Cameroons and Northern Nigeria. Skin snips taken from different parts of the body were weighed on a torsion balance and teased in saline on a slide, the number of microfilariae present in the wet film then being counted. It was found that the concentration of microfilariae was uniform in an area of skin 1 cm. square and was very closely related to the condition of the skin at the point from which the snip was taken, being increased when lichenification was present and diminished when there was fibrous scarring. Both the concentration of microfilariae and the lichenification of the skin were increased on the dorsal surface of the trunk and extensor aspects of the limbs.

The infection was more intense and the spread of microfilariae more advanced in subjects with involvement of the anterior segment of the eye than in those without eye lesions, but no conclusive association could be demonstrated between the development of lesions of the posterior segment and the spread of microfilariae to the

head region. In the authors' view these findings suggest that it may be possible to prevent the development of eye lesions in the individual " by repeatedly reducing the microfilarial intensity at appropriate intervals " with suitable drugs. *R. R. Willcox*

650. **The Chemoprophylaxis of Sleeping Sickness with the Diamidines**

D. GALL. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **48**, 242–258, Sept., 1954. Bibliography.

This review from the West African Institute for Trypanosomiasis Research, Kaduna, Northern Nigeria, surveys the results obtained with diamidines in the prophylaxis of human trypanosomiasis in Nigeria, Sierra Leone, Belgian Congo, French African territories, Portuguese Guinea, Bechuanaland, and Mozambique since 1944. In general, prophylaxis with these drugs has been successful and has even resulted in a decrease in incidence of the disease in the unprotected population, probably owing to reduction of the reservoir of circulating trypanosomes to a level where transmission is negligible.

In Belgian Congo the hope that eradication might be achieved has been unfulfilled owing to the migratory habits of a large section of the population, demanding an ever-widening sphere of prophylaxis, and the appearance of unexpected new foci in regions of low endemicity. In Bechuanaland it appears necessary to give treatment at 2-monthly intervals rather than the longer intervals which have proved satisfactory elsewhere; however, a full assessment of the results has not yet been made. In Mozambique it was concluded that diamidine prophylaxis was unsuitable for a widely dispersed population unless an epidemic occurred.

The most favoured diamidine is pentamidine given intramuscularly, either as the diisethionate or as the dimethyl sulphonate, in doses of 3 to 5 mg. of the base per kg. at intervals of 6 to 12 months. Reduced dosage is generally given to pregnant women, to the frail and sick, and to children. Oral administration has little to recommend it, and the much greater dose of the drug required makes it economically undesirable.

Side-effects are quite common but are usually immediate and mild and constitute no contraindication to mass prophylaxis. On the whole, the diisethionate appears to be less toxic than the other salt. Subjects are usually kept at rest in the shade for 1 or 2 hours after injection and adrenaline is kept at hand in case of accidents. A combination of pentamidine and suramin has also been used, suramin inhibiting the toxic effects of pentamidine.

The failure rate is about 0·1% up to one year after the last injection, the majority of such cases being due to early infections missed at the preliminary survey. Pentamidine-resistance has only once been reported. It is emphasized that careful diagnosis, both in preliminary and subsequent surveys, should be carried out to detect possible cryptic cases, although there is little danger epidemiologically from these as they carry few, if any, circulating trypanosomes. Blood films from substantial samples of the population should be examined at the beginning of each preliminary survey, although the value of this varies from area to area, the greatest value being in the least controlled endemic areas.

It is concluded that diamidine prophylaxis should be regarded as a powerful yet temporary control measure and for its greatest value to be obtained it should be integrated with tsetse eradication and mass survey and treatment. It is, however, of great value alone where tsetse eradication is impracticable or for the protection of special communities such as labour gangs.

I. M. Rollo

651. **Trial of Diallyl-diethyl-aminoethyl Phenol Dihydrochloride (Camoform) in Human Amebiasis**

M. T. HOEKENGA and D. L. BATTERTON. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **3**, 849–851, Sept., 1954. 3 refs.

" Camoform " is a synthetic chemical compound related to the antimalarial drug amodiaquine. It has been shown to be amoebicidal *in vitro* in dilutions as high as 1 in 50,000. In man, during serial administration, 70 to 80% of the daily oral dose is absorbed from the gastrointestinal tract, less than 0·5% being excreted in the urine. There also seems to be considerable localization in the tissues, since when oral administration is stopped the level in the plasma falls by 60% in 3 days, but 15% is still present 3 weeks later. It is usually well tolerated; reports in the literature indicate that treatment with the drug must be given for at least 3 days.

In the present study here reported from La Lima, Honduras, the drug was given to 20 patients, of whom 10 had acute amoebic dysentery and 10 were asymptomatic but were passing cysts. All the adults (18) received 0·5 g. three times a day for 7 days, total dose 10·5 g.; 2 children were given 0·75 g. daily for 7 and 3 days respectively. The patients were followed up for 3 to 4 months. The clinical symptoms were rapidly relieved by the second day, and diarrhoea stopped in 2 to 5 days. The amoebae and cysts disappeared from the stools in a few days, but in one case *Entamoeba histolytica* persisted for 2 weeks after the first dose. In no case was there any evidence of toxicity. In all, 17 of the patients remained free from parasites and symptoms; of the 3 failures, 2 responded to re-treatment. These results are considered good but not spectacular, several other current drugs giving equally good results. But camoform is recommended for further clinical investigation because: (1) it is effective in dysenteric as well as in asymptomatic cases; (2) it is well tolerated; and (3) it can be produced cheaply. *F. Hawking*

652. **The Treatment of Acute Malaria with Single Oral Doses of Amodiaquin, Chloroquine, Hydroxychloroquine and Pyrimethamine**

M. T. HOEKENGA. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **3**, 833–838, Sept., 1954. 10 refs.

At an industrial company's hospital at La Lima, Honduras, over 1,000 cases of acute malaria have been treated with four different antimalarial drugs by the single-dose method during the past few years. Most of

the patients were male and many were partially immune; all drugs were taken by mouth. Chloroquine was given to 320 patients in doses of either 0·4 g. or 0·6 g. of base, amodiaquine to 500 patients in doses of 0·4, 0·6, 0·8, or 1·0 g. of base, hydroxychloroquine in a dose of 1·25 g. to 125 patients, and pyrimethamine (" daraprim ") in a dose of 50 mg. (18 cases) or of 100 mg. (57 cases). Treatment was begun as soon as the diagnosis was confirmed by examination of a blood film.

In nearly all the patients treated with any of the first three preparations the symptoms disappeared in 36 to 48 hours and the patients were able to return to work by the 4th day after treatment. In those given pyrimethamine the response was less rapid, convalescence usually extending to 5 to 7 days; thus pyrimethamine was less efficacious than the other drugs. It was evident that in most cases the dose of 0·4 g. of chloroquine was too small. The parasites disappeared from the blood stream on the average in 26 to 30 hours after the higher doses of the first three drugs and in 38 hours after the larger dose of pyrimethamine.

Of the 320 patients treated with chloroquine 10 did not respond to the single dose but did respond to a 3-day course. Of the 500 patients given amodiaquine, only 3 did not respond; all 3 had received the smallest dose (0·4 g.) and responded well to 1·0 g. Among the 125 patients treated with hydroxychloroquine there were 2 immediate failures, and among the 75 patients treated with pyrimethamine there were 6 immediate failures. The number of known relapses was small, amounting to only 16 out of 1,020 patients treated. All 16 suffered from vivax malaria; 7 had been treated with 0·45 g. of chloroquine, 3 with 0·6 g. of chloroquine, and 6 with 0·4 g. of amodiaquine. There was no evidence of toxicity or intolerance, even when disease conditions other than malaria were also present.

It is concluded that in this region, in which the population is partly immune to malaria, it is practicable to treat most patients with malaria on an ambulant basis with a single oral dose of amodiaquine, chloroquine, or hydroxychloroquine. But a certain number of patients with falciparum infection may have to be kept in hospital for 36 to 48 hours in anticipation of pernicious complications. *F. Hawking*

653. **The Effect of Continuous and Intermittent Primaquine Therapy on the Relapse Rate of Chesson Strain Vivax Malaria**

J. Arnold, A. S. Alving, R. S. Hockwald, C. B. Clayman, R. J. Dern, E. Beutler, and G. M. Jeffery. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 44, 429–438, Sept., 1954. 1 fig., 7 refs.

The experiments here described from the University of Chicago were devised to enable a comparison to be made of the " causal prophylactic " activity of the antimalarial drugs primaquine, the related pamaquin, quinine, chloroquine, and quinacrine. The drugs were administered once daily for 8 days, that is, on the day before exposure to infection, on the day of infection, and on the 6 successive days; each volunteer subject was bitten by 10 mosquitoes heavily infected with the Chesson strain of *Plasmodium vivax*, the resulting infection offering " a greater therapeutic challenge than most naturally acquired infections ". As causal prophylactics quinine (in a dose of 1·64 g. per day),chloroquine (0·275 g. per day), and quinacrine (0·4 g. per day) all proved ineffective, as also did pamaquin (31·5 mg. per day). On the other hand primaquine in doses of 30 mg. per day prevented the ultimate development of clinical malaria in 10 out of 10 subjects, in doses of 15 mg. per day in 8 out of 10 subjects, and in doses of 10 mg. per day in 7 of 10 subjects. No appreciable toxicity from the administration of pamaquin or of primaquine was observed.

Although effective, the method of primaquine administration described would not be of great interest in the practical management of *P. vivax* infections. Hence in a further study a more practical programme of administration was adopted in which the same total dose of primaquine was given in twice-weekly doses each of 30 mg. for 4 weeks beginning on the day of infection. In this study 2 of 12 subjects developed patent malaria after the completion of treatment. In these 2 cases the symptoms were controlled by giving 1 g. of chloroquine base during the first 24 hours of the attack; after a second course of primaquine there was no further relapse. Subinoculation from 2 subjects in this group on the 9th and 15th days into a second group of 4 non-immune subjects did not result in infection, showing that there was no development of trophozoites in the " subpatent " infections. The effect of once-weekly administration was then studied. When 30 mg. of primaquine was given weekly for a total of 15 weeks, 2 out of 5 patients remained free of malaria 21 and 52 weeks after the last dose of the drug; the remaining 3 relapsed after the first course of the drug. Chloroquine had to be given to control the parasitaemia, which occurred within 2 weeks in all cases and at various times afterwards in 4 out of the 5. However, when 300 mg. of chloroquine base was given concurrently with the weekly 30-mg. doses of primaquine, 8 of 10 subjects remained parasite-free and asymptomatic during therapy and for 15 to 51 weeks after the last dose of the drug.

In prolonged toxicity studies primaquine, 30 mg. base, and chloroquine, 300 mg. base, were given weekly to 60 subjects for 12 months and to 37 others for 9 months. No toxic effects were observed and the blood and urine remained normal.

The authors conclude from these results that semi-weekly treatment with primaquine, or weekly treatment with primaquine plus chloroquine, would appear to have considerable value in situations analogous to that faced by troops returning from Korea.

[It should be remembered, however, that the results obtained were with infections with a strain which relapses early and that modifications in therapy might be necessary in treating strains, such as the Madagascar strain, the tissue forms of which can remain latent for 30 to 40 weeks. The original paper should be consulted for definitions of the special terms " causal prophylaxis ", " prophylactic cure ", and " suppressive cure " used by the authors to describe the action of different dosage schedules.] *I. M. Rollo*

Allergy

654. **Effectiveness of a Portable Electrostatic Precipitator in Elimination of Environmental Allergens and Control of Allergic Symptoms**

S. FRIEDLAENDER and A. S. FRIEDLAENDER. *Annals of Allergy* [*Ann. Allergy*] **12**, 419–428, July–Aug., 1954. 2 figs., 9 refs.

The authors describe an apparatus for the elimination of environmental allergens from house air, which depends on the principle of electrostatic precipitation of airborne particles. The machine can be run on the usual domestic electric current, weighs 40 lb. (18 kg.), has an air intake and output of 200 c. ft. (5·9 c. metre) per minute, and precipitates nearly 100% of particles ranging from 0·001 to 100 μ in diameter. Pollen introduced into a room was removed satisfactorily. In a clinical trial in which 30 patients suffering from hay fever or asthma took part 9 out of the 12 who were sensitive to pollen obtained excellent relief within 10 to 30 minutes of entering the air-cleaned room. The results in dust-sensitive patients were not uniform. *H. Herxheimer*

655. **Seasonal Periodicity in Atmospheric Mould Spore Concentrations.** [In English]

M. RICHARDS. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] 7, 357–366, 1954. 4 figs., 11 refs.

Petri dishes containing Sabouraud's maltose agar have been exposed for 10 minutes at 10 a.m. every week-day for the last 3 years at St. David's Hospital, Cardiff. Nearly 100 genera have been identified, although about 95% of the mould catch is made up of only 11 genera. Five of these (*Cladosporium*, *Epicoccum*, *Alternaria*, *Botrytis*, and *Pullularia*) have a seasonal periodicity, 3 others (*Aspergillus*, *Oospora*, and *Candida*) show a much less marked variation from one season to another, and the remaining 3 (*Penicillium*, *Phoma*, and *Sporotrichum*) have a non-seasonal distribution. The seasonal moulds are in highest concentration in the summer months from June to September. *Cladosporium* is the predominant genus, constituting 38% of the total catch (more in rural areas), 78% of catches of this genus occurring during the period July to September. *A. W. Frankland*

656. **Long-term Control of Severe Bronchial Asthma with Oral Cortisone**

R. S. SAVIDGE and W. BROCKBANK. *Lancet* [*Lancet*] 2, 889–893, Oct. 30, 1954. 5 figs., 7 refs.

The results obtained with cortisone in the treatment of 13 cases of severe bronchial asthma of at least 2 years' duration are described in this paper from Manchester Royal Infirmary. The dose of cortisone, which was given by mouth, did not exceed 100 mg. daily, and the duration of treatment was 7 to 80 weeks. In 6 cases there was great improvement; for example, one patient, formerly bedfast, was able to lead a life of limited activity, while another, who had repeatedly lost time from work, experienced a relapse on one occasion only during a year's treatment, when a blank solution was substituted for the cortisone. Improvement, mostly subjective, was noted in 4 other patients. Of the remaining 3 patients, 2 died while receiving cortisone [see Abstract 657], and one, who failed to show any improvement, died from bronchopneumonia 7 months after the course of cortisone was completed. The commonest side-effect was gain in weight. A moderate rise in blood pressure was noted in 3 patients, while in 3 others there were episodes of pneumonitis during treatment which responded to administration of an antibiotic. Most of the patients had a relapse within a short time of the cessation of treatment. *R. S. Bruce-Pearson*

657. **Two Deaths during Cortisone Treatment of Bronchial Asthma**

R. S. SAVIDGE and W. BROCKBANK. *Lancet* [*Lancet*] 2, 893–895, Oct. 30, 1954. 2 figs., 10 refs.

In the previous paper [see Abstract 656] the authors reported 2 deaths from chronic asthma during cortisone treatment; in the present paper they describe these 2 cases in detail. The first patient, a man aged 45 with 20 years' history of bronchitis, developed asthma which did not respond to the usual methods of treatment. At first symptoms were relieved by cortisone, but later there were repeated relapses, although he was receiving a maintenance dose of 12·5 to 75 mg. daily. He died in status asthmaticus after 5 months' treatment while receiving a dose of 75 mg. daily. The second patient, a man aged 29, had had asthma almost continuously for 3 years. Improvement followed administration of cortisone, although the patient was not entirely free from spasm. He was later readmitted to hospital and died in status asthmaticus, the maintenance dose at the time of death being 75 mg. daily.

The authors consider that suppression of spontaneous adrenal activity by cortisone therapy might have been partly responsible for death in these 2 cases. They cite 8 similar cases from the literature, and conclude that "cortisone treatment is dangerous to life in some undefined types of asthma".

[Though this conclusion may be correct, no evidence in support of it is provided by these 2 cases. Both patients had severe asthma, and death appears to have been the direct result of the disease.] *R. S. Bruce-Pearson*

658. **Rape Pollen Allergy. Report of a Case.** [In English]

H. COLLDAHL. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] 7, 367–369, 1954. 4 refs.

The case of a farmer who had conjunctivitis, rhinitis, and asthma due to rape pollen (*Brassica napus*) is described from the University Hospital, Lund, Sweden. This is the first published account of sensitivity to the pollen of a plant belonging to the *Cruciferae* family. *A. W. Frankland*

Gastroenterology

659. **An Interim Report upon the "Second Look" Procedure for Cancer of the Stomach, Colon, and Rectum and for "Limited Intraperitoneal Carcinosis"**
O. H. WANGENSTEEN, F. J. LEWIS, S. W. ARHELGER, J. J. MULLER, and L. D. MACLEAN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 257–267, Sept., 1954. 5 figs., 13 refs.

This is an account from the Hospital of the University of Minnesota of the treatment of 103 patients with visceral cancer in whom regional lymph-node metastases were discovered and removed at the primary operation. After 6 to 8 months they were subjected to a "second look", the abdomen being again explored and any residual growth removed, if possible, and further operations were performed at approximately the same intervals until no growth was found. This procedure was initially employed in cases of large carcinomata of the colon adherent to the surrounding structures but with no lymph-node involvement. It was, however, shown to be unnecessary, as no residual cancer was found at the second operation. Six patients with cancer at other sites who were found to have residual growth at the second operation have at subsequent operations been found to be free from growth.

[This procedure in general is not one that would appeal to patients in Great Britain and, although admittedly experimental, would seem to have little to recommend it. Macroscopic, not microscopic, evidence of growth is taken as the criterion for excision at the secondary operation and the interval between operations is an arbitrary one. Failure to achieve much with hepatic metastases is admitted and is attributed to inadequate liver resection, but wider excision has obvious drawbacks and possibly no advantages.] *Guy Blackburn*

660. **Studies of Uropepsinogen Excretion in Gastrointestinal Disorders**
W. SIRCUS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 291–306, July, 1954. 27 refs.

With a substrate made from dehydrated human plasma, the excretion of uropepsinogen has been measured in normal subjects and in cases of duodenal ulcer, gastric ulcer, secondary dyspepsia, carcinoma of the stomach, partial and total gastrectomy, haematemesis, iron-deficiency anaemia, and pernicious anaemia.

The mean output of uropepsinogen in duodenal ulcer was almost double that found in normal subjects, and change in the state of the lesion, clinically assessed, was accompanied by a corresponding rise and fall of uropepsinogen excretion, with differences between the sexes in the degree of change. The mean output in cases of gastric ulcer was within normal limits, when patients with an associated duodenal ulcer were excluded. No uropepsinogen was excreted by patients who had had total gastrectomy, or by the majority of those who had had partial gastrectomy. Stomal ulcers existed in the 2 patients who showed a relatively high excretion. In patients suffering from haematemesis of unknown origin, a high output of uropepsinogen showed a significant correlation with the subsequent disclosure of a duodenal ulcer. In patients who suffered from dyspepsia not due to disease in the gastrointestinal tract, with one exception, the excretion rate was normal.

In cases of iron-deficiency anaemia the excretion of uropepsinogen was always less than half the mean output of the controls, and in some cases was absent. A close correlation existed between the uropepsinogen output and the response of the parietal cells to a triple-dose histamine test. The mean excretion of uropepsinogen in pernicious anaemia was extremely low, and more than half the patients produced no measurable quantity. One of the group excreting uropepsinogen also excreted a small amount of hydrochloric acid in response to a triple-dose histamine test.

Patients who had carcinoma of the stomach excreted less uropepsinogen than normal subjects, but the finding has no diagnostic value.

It is considered that the measurement of uropepsinogen is of value in clinical investigation, and as a research tool for further gastrointestinal studies.—[Author's summary.]

661. **Studies on Recurrent Aphthae: Evidence that Herpes Simplex is not the Etiological Agent, with Further Observations on the Immune Responses in Herpetic Infections**
M. M. STARK, S. KIBRICK, and D. WEISBERGER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 261–272, Aug., 1954. 29 refs.

In this paper from the Harvard Medical School additional evidence is presented to show that the virus of herpes simplex is not the agent responsible for recurrent aphthae. Examination of 101 sera from 62 subjects with a history of recurrent aphthae, herpetic infection, or both, for antibodies against herpes simplex was carried out by means of complement-fixation or virus-neutralization tests or both. Of the 59 subjects tested for complement-fixing antibodies, 40 gave a positive result, including 5 patients with a questionable past history of herpes and 10 with no knowledge of past herpetic infections, this emphasizing the frequency of mild or subclinical infections with this virus. The incidence of herpes complement-fixing antibodies among subjects with recurrent aphthae was no higher than that in a control group with no history of this disorder. It was found that sera containing no herpetic complement-fixing antibodies occasionally contained neutralizing antibodies against this virus. Of 30 patients with recurrent aphthae, 11 had no demonstrable antibodies against herpes simplex; 7 of these patients developed a recurrence of their lesions while under observation, yet in none of

them was there a rise in titre of herpes antibodies during convalescence.

The authors discuss previous work on this subject and point out that whereas herpes virus is fairly easily recoverable from herpetic infections, it has never been found possible to recover the virus from cases of recurrent aphthae. Although there have been a few instances in which the virus of herpes has been isolated from the saliva of patients with recurrent aphthae, it has usually been shown that these patients had neutralizing antibodies in their serum at the time of their attack, suggesting that they already had or were recovering from an attack of herpes. Similarly in the few cases of recurrent aphthae in which herpes antibodies have been demonstrated in the blood, the initial antibody titre has usually been high enough to suggest a previous attack of herpes. The authors conclude that their present study and the work of other authors indicate that the virus of herpes simplex is not the aetiological agent in recurrent aphthae. *R. F. Jennison*

STOMACH AND DUODENUM

662. **Hiatal Anomalies and the Cardiac Reflux. Maldevelopment of the Cardiac Fornix.** (Zur Frage der Hiatusanomalien und des Kardiarefluxes. Kardia-Fornix-Fehlanlagen)
F. ROBERT and T. HOFFMANN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **81**, 255–270, Sept., 1954. 13 figs., 16 refs.

The authors discuss a condition described by Lortat-Jacob and Robert (*Arch. Mal. Appar. dig.*, 1953, **42**, 750) which presents a clinical picture resembling that of hiatus hernia and produces *x*-ray appearances at the gastric cardia which are often difficult to interpret. For example, longitudinal folds may be seen passing from the stomach into the lower end of the oesophagus, and it is impossible to say whether these are thick and inflamed oesophageal folds or thin gastric ones. The difficulty lies in deciding in these cases whether there is or is not gastric mucosa above the diaphragm. Radiography shows no displacement of the stomach through the diaphragm. From direct and indirect evidence the authors postulate a " germ-layer defect " which leads to the loss of the oesophago-gastric angle. This angle, which results from the oblique entry of the oeophagus into the stomach, acts as a bar to vomiting; in normal persons expulsion of the gastric contents depends on special muscles passing from the hiatus to the cardia which (on the analogy of the levator ani) pull the oesophago-gastric junction into the stomach. In persons who suffer from gastro-oesophageal reflux but no definite hernia, the stomach is permanently in the " vomiting position ".

Since 1951, 25 cases of this kind have been diagnosed radiologically at the Hôpital Broussais, Paris, of which 16 have so far come to operation; the findings in these cases are tabulated. At operation the oesophagus was drawn down and sutured to the crus of the diaphragm and to the fundus of the stomach (oesophago-gastropexy) so as to restore the important normal gastric angle. The widened oesophageal hiatus was also sutured and narrowed. It is stated that " the majority " of the patients were cured, and reflux could no longer be demonstrated. The follow-up period, however, has been too short to allow of prediction as to whether the operation will have a permanent place in surgery. The authors believe that in the past this gastric disorder has too often been dismissed as merely " functional ".

Denys Jennings

663. **The Inhibitory Action of Sucrose on Gastric Digestive Activity in Patients with Peptic Ulcer**
J. N. HUNT. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **103**, 161–173, 1954. 5 figs., 24 refs.

At Guy's Hospital, London, the author, using a modification of his serial test-meal technique, studied the effect of increasing concentrations of sucrose in the meal on the gastric emptying time and secretory response of: (1) healthy subjects, (2) patients with duodenal ulcer, and (3) patients with gastric ulcer. In all three groups it was found that as the concentration of sucrose in the test meal was raised, so the volume of the gastric contents at 30 minutes increased. The secretion of parietal and non-parietal components and the output of pepsin in the presence of varying concentrations of sucrose generally followed the same pattern in patients with ulcer as in controls, anomalies in 2 of the latter apparently being due to an increased secretory response to distension by the meal, which counteracted the tendency of the sucrose to inhibit parietal secretion. Among the patients with peptic ulcer there was much variation in the volume of non-parietal secretion as compared with healthy subjects.

The author concludes that the mechanisms whereby sucrose delays gastric emptying and inhibits the parietal secretion in patients with ulcer are similar to those in healthy subjects, so it is unlikely that the failure of the latter mechanism is responsible, as has been suggested, for the high proportion of hypersecretors among patients with duodenal ulcer. *J. Naish*

664. **Gastro-duodenal Haemorrhage in the Elderly**
A. W. BRANWOOD and R. F. ROBERTSON. *Edinburgh Medical Journal* [*Edinb. med. J.*] **61**, 305–310, Sept., 1954. 5 refs.

A series of 116 cases of gastro-duodenal haemorrhage from all causes in patients over the age of 60 treated at the Royal Infirmary, Edinburgh, between 1944 and 1951 are reviewed to determine factors in the prognosis. Out of this total, 84 cases were attributable to chronic peptic ulcer, with a relatively high incidence of gastric ulcer. Gastric carcinoma was remarkably rare (4 cases), and there was no case of portal hypertension. Only 8 cases had been treated surgically, but this may have been due to the fact that operative treatment of gastro-duodenal haemorrhage was not usual during the period concerned, and to the reluctance of surgeons to operate on the elderly. The over-all mortality was 19%. The mortality rate for gastric ulcer was almost six times that for duodenal ulcer; also recurrence of bleeding

was less frequent with the latter. Among 86 cases without recurrence of bleeding there were no deaths. The mortality in cases treated medically after recurrent bleeding from peptic ulcer was 20 out of 22, and the authors consider, in retrospect, that surgery should have been practised more often.

It is stressed that early diagnosis is difficult in cases of gastro-duodenal haemorrhage, but, particularly where bleeding recurs, there is a strong probability that chronic peptic ulceration is present. For recurrence of bleeding in elderly patients it is considered that emergency gastrectomy offers almost the only chance of survival; where the cause is a gastric ulcer such a measure is imperative. Methods of early detection and management of further bleeding are discussed. In considering the question of operation it is urged that age and concomitant disease should not be allowed to influence the decision unduly.

J. N. Agate

LIVER AND GALL-BLADDER

665. **The Pathogenesis of Ascites and a Consideration of its Treatment**

J. L. MADDEN, J. M. LORÉ, F. P. GEROLD, and J. M. RAVID. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 385–391, Oct., 1954. 14 figs., 10 refs.

At St. Clare's Hospital, New York, the vascular anatomy of the normal liver and of the diseased liver was studied post mortem, coloured solutions of neoprene latex being injected into the liver, which was then corroded with hydrochloric acid.

In cirrhosis of the liver with irreversible ascites there was an increase in the volume of the portal venous and the hepatic arterial vascular beds, with constriction of the hepatic venous tree. There was also histological evidence of obliterative fibrosis of the smaller branches of the hepatic veins. In cirrhosis without ascites or with reversible ascites a decrease in all the vascular beds of the liver was noted, especially those of the portal and hepatic veins. In the presence of multiple malignant metastases there was an increase in the hepatic arterial bed. It is suggested that ascites is due to obstruction of the outflow tract of the liver by obliterative fibrosis of the hepatic veins in cirrhosis with irreversible ascites, and by intrahepatic cellular oedema in cirrhosis with reversible ascites.

P. C. Reynell

666. **Portal-systemic Encephalopathy. Neurological Complications of Liver Disease**

S. SHERLOCK, W. H. J. SUMMERSKILL, L. P. WHITE, and E. A. PHEAR. *Lancet* [*Lancet*] **2**, 453–457, Sept. 4, 1954. 3 figs., 11 refs.

The occurrence of neurological disorders in association with disease of the liver has long been recognized—coma as the terminal phase of many hepatic diseases and the peculiar syndrome of Kinnier Wilson's disease may be cited as examples. The present paper from the Postgraduate Medical School of London, while mentioning coma, deals particularly with other neurological disturbances, very varied in character, occurring in 18 patients with liver disease. The symptoms and signs were so numerous that no special and recognizable syndrome can be set out—they included apathy, confusion, grimacing, "flapping" tremor of the arms, and many others of indefinite nature. Although usually transient, in some cases these signs preceded the onset of coma.

The suggestion is strongly made that the cause of these signs is the diversion of portal venous blood through collateral channels, so that certain nitrogenous substances which are normally detoxicated during their passage through the liver escape directly into the systemic circulation. Biochemical observations showed in all cases a high content of ammonia in the blood, this being the only abnormality constantly detected. As regards treatment, the authors have given a good trial to glutamic acid and sodium glutamate, as recommended by Walshe (*Lancet*, 1953, **1**, 1075; *Abstracts of World Medicine*, 1954, **15**, 35) for hepatic coma, but the results were negative and the ammonia level of the systemic blood remained unchanged.

The authors warn mildly [but with good reason] against the excessive use of high-protein diets, casein hydrolysates, and amino-acid supplements in the treatment of liver disease in view of the relation between high blood ammonia levels and neurological complications. They suggest the term "portal-systemic encephalopathy" to describe these neurological disturbances.

J. W. McNee

667. **The Distribution of the Hepatic Artery within the Liver.** (Distribution de l'artère hépatique dans le foie)

C. COUINAUD. *Acta anatomica* [*Acta anat.* (*Basel*)] **22**, 49–81, 1954. 15 figs., 21 refs.

The distribution of the hepatic artery within the liver was studied at the anatomical laboratories of the Faculty of Medicine, Paris, in 97 injected specimens and in several fresh livers. The prepared organs were injected with a solution of "vinylite" in acetone, and corrosion preparations were made with hydrochloric acid. [No details of technique are given.] The author's findings were as follows. The liver is divided into eight segments, and the branches of the hepatic artery supplying these segments correspond closely with the distribution of the portal vein and bile duct. These arteries are described and their variations are recorded and illustrated. The hepatic artery may be single, double (18 cases), or triple (3 cases). In 22 specimens the left gastric artery was found to give off a large branch to the liver, in every case to the left lobe, but the number of segments it supplied varied; five variations in this artery are described. Other points which are recorded are the variations in the origin of the cystic artery, the relation of the arteries to the veins and biliary ducts, and the arterial anastomoses at the hilum; these are discussed from the surgical point of view. (In a long footnote to his paper the author compares his findings with those of Healey *et al.* (*J. int. Coll. Surg.*, 1953, **20**, 33; *Abstracts of World Medicine*, 1954, **15**, 394), which were published while the present paper was in proof, and comments on some of the main differences.)

[Since the author's paper contains many illustrations and tables showing the numerous variations of all the

above-mentioned structures and their incidence, it is impossible to enumerate the detailed findings in an abstract, and for these the original paper should be consulted.] *D. B. Moffat*

668. **The Hepatic Blood Flow and Splanchnic Oxygen Consumption in Alcoholic Fatty Liver**
B. J. KESSLER, J. B. LIEBLER, G. J. BRONFIN, and M. SASS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1338–1345, Oct., 1954. 1 fig., 18 refs.

Investigations were carried out at the Veterans Administration Hospital, Brooklyn, New York, to determine whether fatty infiltration of the liver in alcoholic patients diminishes the blood flow through this organ, and if so whether the flow was improved after a period of treatment during which disappearance of the fat might be expected to take place. In all, 12 alcoholic subjects and 17 presumably normal controls were studied by the "bromsulphalein" method described by Bradley *et al.* (*J. clin. Invest.*, 1945, **24**, 890), a cardiac catheter being passed via the vena cava into the right hepatic vein; the oxygen content of the blood in the hepatic vein was also estimated and needle biopsy of the liver was performed in each case.

The results did not show that there was any significant alteration in blood flow through the liver before and after treatment, nor that fatty infiltration of the liver causes any impairment of the total hepatic blood circulation. (It is stressed that in every case of alcoholism studied, so far as could be determined, actual cirrhosis of the liver was absent.) It appeared, however, that in the alcoholic subjects the oxygen uptake in the liver was greater than normal, and the authors suggest that the finding of a lowered hepatic venous oxygen saturation may be of significance as representing some anoxia contributing to the centrilobular cellular changes seen in alcoholic livers. *Thomas Hunt*

669. **Needle Biopsy of the Liver. IX. Further Experiences with Malignant Neoplasm**
J. WARD, L. SCHIFF, P. YOUNG, and E. A. GALL. *Gastroenterology* [*Gastroenterology*] **27**, 300–306, Sept., 1954. 6 figs., 5 refs.

Needle biopsy of the liver was performed on 111 patients subsequently shown to have neoplasm of one type or another in the liver. The needle biopsy specimen demonstrated the lesion in 74% of these patients. Needle biopsy is an important adjunct to the clinical investigation of patients with suspected hepatic neoplasm.—[Authors' summary.]

670. **Chronic Idiopathic Jaundice with Unidentified Pigment in Liver Cells. A New Clinicopathologic Entity with a Report of 12 Cases**
I. N. DUBIN and F. B. JOHNSON. *Medicine* [*Medicine (Baltimore)*] **33**, 155–197, Sept., 1954. 5 figs., 46 refs.

Out of approximately 4,000 liver biopsy specimens from cases of hepatic disease filed at the Armed Forces Institute of Pathology, Washington, D.C., 12 were found to show changes which led to the discovery of a very uncommon, but essentially benign, pigmentary disorder of the liver. Of the 12 patients, 9 were members of the U.S. Armed Forces when they developed the disease and 3 were civilians. All the former were young—from 20 to 26 years of age—while the 3 civilians were all 42 years of age.

These 12 cases are considered to exemplify a hitherto undescribed clinical and pathological entity, somewhat similar to, but not identical with, what has been called "constitutional hyperbilirubinaemia", chronic juvenile jaundice, or Gilbert's disease. It is a true jaundice, with abundant bile pigment in the plasma, giving always a direct and sometimes also an indirect van den Bergh reaction. The urine is dark in colour, and liver function tests often give abnormal results. The gall-bladder cannot be visualized by cholecystography, and yet the jaundice is certainly not obstructive. Laparotomy in 8 of the cases showed the liver to be smooth and of a grey-black or green-black colour which was explained only on histological examination. The patients could not be said to be well, but they were not seriously ill and none of them died. This matter of prognosis is important since before liver biopsy was performed the condition was often confused with the progressive and serious sequelae of infective hepatitis.

On histological examination of the liver biopsy material [of which excellent photomicrographs are reproduced in colour] the liver in each case was free from obvious pathological change, but the cells were found to be filled with a dull, dark brown pigment. The nature of the pigment remains unknown; it is certainly not haemosiderin, and the authors can only suggest that it is some very unusual pigment derived through bilirubin (abundantly present in the blood plasma in all cases) from haemoglobin as a result of an inborn metabolic defect in the liver. There is a possibility that the pigment belongs to the group of mesobilifuscins, such as have been found in a peculiar hereditary disease of sheep.

[Altogether, this was a very interesting piece of detection in which the discovery of the unusual pathology in the first place led to a study of the clinical aspects of the cases from which the material was derived.]
J. W. McNee

671. **Recurrent Pyogenic Cholangeitis**
J. COOK, P. C. HOU, H. C. HO, and A. J. S. MCFADZEAN. *British Journal of Surgery* [*Brit. J. Surg.*] **42**, 188–203, Sept., 1954. 16 figs., 17 refs.

This study of recurrent pyogenic cholangitis is based on the findings in a series of 90 patients suffering from the disease admitted to the Queen Mary Hospital, Hong Kong, in the years 1950–2. All the patients were Chinese. The disease is common in Hong Kong; it is frequently accompanied by the formation of gall-stones and occurs in younger persons and in a considerably larger proportion of males than is usual with gall-stones among Europeans.

The chief symptoms are fever, pain, and jaundice. The fever is irregular and may be associated with rigors. The pain is chiefly in the right hypochondrium. Jaundice usually appears after one or more attacks, and is rarely deep. In half the cases the liver is enlarged and in one

case out of every six the spleen is larger than normal. There is a leucocytosis of the polymorphonuclear type. The urobilinogen content of the urine is increased even when jaundice is absent. The gall-bladder is often enlarged and may be palpable. The stones may be large or small, are commonly found in the biliary ducts, and are usually composed of a soft core of bilirubin and a harder coating of calcium bilirubinate. Cholesterol is found only in a small proportion of the stones.

In specimens obtained by liver puncture and at operation in the authors' series the predominant organisms were found to be *Escherichia coli* and an anaerobic streptococcus. The biliary ducts were thickened and dilated, often in an irregular manner. The authors consider the infection of the ducts to be primary and that of the gall-bladder secondary. At a late stage, after many recurrent attacks, a monolobular cirrhosis of the liver results. The main lines of treatment are to diminish the infection by administering antibiotics and then to operate for the purpose of removing the stones and draining the ducts. Cholangiography is useful as a means of making sure that the ducts have been properly emptied of stones. In young persons in whom stones may not yet have formed the authors have hitherto pursued a conservative line of treatment, but they now incline to the view that exploration is the wiser course in such cases. Operation is not curative, but palliative; the infection does not yield permanently to antibiotics and the prognosis is poor. *Zachary Cope*

672. **Osteoporosis in Patients with Biliary Fistulae.** (Остеопорос у больных с наружными желчными свищами)
S. A. Reĭnberg. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **32**, 45–49, Sept., 1954. 4 figs., 4 refs.

In 1905 Pavlov described a condition of softening of the bones in some of his dogs in which intestinal or pancreatic fistulae, or more often fistulae of the gall-bladder or bile-ducts, had been made; it was never found in dogs with gastric fistulae. The bones chiefly involved were the ribs, spine, pelvis, pectoral girdle, and skull. At first Pavlov believed that the long bones were never involved, but he later observed, in severe cases, osteoporotic changes in these also. Moiseev, after careful histological examination of the changes, expressed the opinion that they were analogous to those found in osteomalacia. Pavlov explained the condition as being due to loss of digestive juices and their salts, and the effect of exposure to damp and cold. Nikolaev regarded them as being due to the loss not only of salts, but also of protein and phosphorus compounds.

Long-standing biliary fistulae in human beings are rare nowadays, as they are usually successfully dealt with surgically. However, the author, who is Director of the Faculty of Radiology at the Central Institute, Moscow, has confirmed the existence of osteoporosis in 4 cases of biliary fistula of from 1½ to 11 months' duration. The patients had shown no subjective or objective symptoms. The amount of bile lost daily seemed to have no relation to the degree or rate of development of the osteoporosis.

[This study is based purely on radiological evidence; it would have been of greater value if biochemical and pathological investigations had been combined with it. Four reproductions of radiographs accompany the text, but there are no reports of determination of the serum calcium, phosphorus, or alkaline-phosphatase levels. Nor is loss of fat-soluble vitamin D mentioned as a possible cause of the condition, although it is stated to resemble osteomalacia.] *L. Firman-Edwards*

INTESTINES

673. **Chronic Ulcerative Colitis and Regional Enteritis —Their Allergic Aspects**
A. H. Rowe and A. Rowe. *Annals of Allergy* [*Ann. Allergy*] **12**, 387–402, July–Aug., 1954. 3 figs., 24 refs.

As their results have accumulated, the authors have become more and more convinced that atopic allergy is a primary cause of chronic ulcerative colitis and regional enteritis. During the past 16 years they have studied 138 cases of ulcerative colitis. In 45% of these food allergy was found and in 3% allergy to pollen. The offending food factors in the majority of cases were milk, fruits, chocolate, and condiments.

The patients were treated with a fruit-free and milk-free elimination diet, and excellent results are claimed in 45% of all patients. There were 9 deaths during the first 8 years of the study, compared with no deaths during the second 8 years, and during this period only 2 patients had to undergo ileostomy or colectomy. Some typical case histories are given.

[Although some of the successes may have been due to additional therapeutic measures—in 17 cases cortisone was given—the results seem to be impressive.]
H. Herxheimer

674. **Justification for Appendicectomy in Chronic Appendicitis**
I. McLennan and J. K. Watt. *British Medical Journal* [*Brit. med. J.*] **2**, 736–738, Sept. 25, 1954. 1 fig., 8 refs.

An investigation was carried out at Glasgow Royal Infirmary to determine whether appendicectomy in patients complaining of pain in the right iliac fossa is justified by results. A total of 138 males and 429 females were subjected to appendicectomy between 1946 and 1950, and of these, 97 males and 316 females were followed up. It was found that the results were better in females than in males, the cure rate for females being 83·5% compared with 74·2% for males. In only about 15% of the patients was epigastric pain associated with pain in the right iliac fossa.

The commonest type of error was due to misinterpretation of symptoms in males, the ultimate diagnosis in 10% of these being duodenal ulcer. The pain was due to a gynaecological lesion in only 4 of the females and to cholecystitis in 6.

[The investigation dealt only with the cure of pain by appendicectomy. No information is provided on the mobility of the caecum, caecal stasis, or the histology of the appendix.] *K. Whittle Martin*

Cardiovascular System

675. **Studies on the Use of Ethaverine in the Treatment of Angina Pectoris**
D. L. SIMON, A. IGLAUER, and R. C. SCOTT. *American Heart Journal* [*Amer. Heart J.*] **48**, 624–628, Oct., 1954. 20 refs.

A trial of ethaverine, the ethyl analogue of papaverine, in the treatment of 22 patients with established angina pectoris is reported in this paper from the Cincinnati General Hospital, Cincinnati, Ohio. A control period of 6 weeks was followed by two similar periods during which the patients received either ethaverine in a dosage of 50 mg. 4 times a day or a placebo of identical appearance. The doctor was unaware which of these was being taken, but all patients received a complete course of treatment with both the drug and the placebo. The results were analysed when the trial was completed. The patients recorded their daily consumption of tablets of nitroglycerin, and at intervals 12-lead electrocardiograms were taken and exercise tolerance tests carried out.

Statistical analysis of the consumption of nitroglycerin tablets did not reveal any significant difference between the number taken each week during ethaverine treatment and the number taken during administration of the placebo. The consumption of nitroglycerin during both treatment periods was, however, slightly less than in the control period; this decrease was a little more marked with ethaverine than with the placebo, but in neither case was it of statistical significance.

Five patients were given ethaverine in a dosage of 100 mg. 4 times a day; 4 of these took fewer nitroglycerin tablets while receiving the placebo than while they were receiving the drug. No change was observed in the results of exercise tolerance tests or in the electrocardiogram in either group of patients during either treatment period.

The authors conclude that the slight reduction in the consumption of nitroglycerin was attributable, in part, to psychological factors, and that ethaverine does not appear to be of value in the treatment of angina pectoris, although statistically significant results might be obtained with a higher dosage in a larger series of cases.

Charles Rolland

676. **Endocardial Fibroelastosis: a Factor in Heart Disease of Obscure Etiology. A Study of 20 Autopsied Cases in Children and Adults**
W. A. THOMAS, R. V. RANDALL, E. F. BLAND, and B. CASTLEMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 327–338, Aug. 26, 1954. 4 figs., 38 refs.

The authors, reviewing the post-mortem reports of all cases of heart disease of obscure aetiology out of 10,000 cases coming to necropsy at the Massachusetts General Hospital in the past 25 years, have differentiated a group of 20 cases of chronic heart disease with hypertrophy of uncertain aetiology and extensive fibroelastic thickening of endocardium and subendocardium. These they divided arbitrarily into three subgroups: infantile, childhood (2 to 16 years), and adult cases.

In the 4 infantile cases the patient had had symptoms for some months before death. There was marked cardiac hypertrophy with endocardial fibroelastosis overlying a relatively normal myocardium, but no evidence of any inflammation or thrombosis. The authors postulate that in these cases the aetiology was congenital. In the childhood group, also of 4 cases, the findings were similar except for later onset of symptoms and slighter degree of hypertrophy, and it is considered that these also were congenital in origin.

The 12 adult cases were morphologically similar to the other types of case, but in 9 of them mural thrombi were present. There was no gross myocardial fibrosis or evidence of inflammation. The history was longer than in the younger groups, congestive failure was prominent, and some patients had a family history of obscure heart disease. The authors discuss the aetiology of this type of heart disease and conclude that, despite the lack of specificity of the fibroelastosis and the late onset of symptoms, it too is congenital in origin. The relationship between the pathological changes and symptoms is also discussed and comparisons are made with other obscure heart diseases.

The 20 case histories are presented in detail.

D. Goldman

677. **Renal Haemodynamics in Chronic Constrictive Pericarditis.** (L'hémodynamique rénale au cours des péricardites constrictives chroniques)
J. HIMBERT, A. THÉARD, P. GELÉ, and L. SCÉBAT. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 733–746, Sept., 1954. 7 figs., 3 refs.

Measurements of the renal plasma flow (R.P.F.) and glomerular filtration rate (G.F.R.) were made on 15 patients with chronic constrictive pericarditis, of whom 9 had obvious oedema and 8 of these ascites. The average R.P.F. was low in the group of 6 patients without oedema, and even lower in the group of 9 with oedema. A less significant reduction in the average figures for G.F.R. was noted, the values for some individuals coming within the normal range. The filtration fraction thus tended to be high in the worst cases.

In most cases cardiac catheterization was also carried out. Calculation of the proportion of the cardiac output going to the kidneys showed the average for both groups to be lower (15% and 16% respectively) than in normal controls (22%). No correlation was found between renal blood flow and systemic venous pressure—unlike patients with valvular heart disease [see Abstract 678], in whom a low renal blood flow accompanied high venous pressure.

Six patients underwent pericardectomy, all showing very satisfactory clinical improvement. In most of these cases investigation after the operation showed an increase in R.P.F. and in G.F.R. However, the rise in cardiac output was even more striking, so that the proportion of cardiac output going to the kidneys tended to fall. *J. A. Cosh*

CHRONIC VALVULAR DISEASE

678. **Renal Haemodynamics in Valvular Heart Disease.** (L'hémodynamique rénale dans les cardiopathies valvulaires)

J. HIMBERT, A. THÉARD, P. GELÉ, L. SCÉBAT, and J. LENÈGRE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 747–766, Sept., 1954. 12 figs., 35 refs.

Measurements of the renal plasma flow (R.P.F.) by determining PAH clearance, and of the glomerular filtration rate (G.F.R.) by determining mannitol clearance, were made on 60 patients with varying degrees of disability caused by valvular heart disease. None had evidence of renal disease, and few were over 50 years of age. They were classified in five groups: (I) with normal heart or with lesions causing no disability; (II) with pulmonary congestion due to mitral stenosis, but without heart failure; (III) recovering from congestive heart failure; (IV) in congestive heart failure without oedema; and (V) in congestive failure with oedema.

There was a progressive diminution in the average R.P.F. from Group I to Group V, with some overlapping of the individual values between groups: in all cases in Group V, however, the values were well below the lowest limit of normal. A similar diminution in the average G.F.R. was noted, but this fell to a smaller degree than the R.P.F., so that the filtration fraction rose progressively from Group I to Group V. In Group V, the only group with oedema, the G.F.R. was not significantly lower than in Group IV. No clear relationship between the G.F.R. and the presence of oedema was found, for in 2 out of the 9 patients with oedema the G.F.R. was virtually normal, whereas in some patients in Group III who had recovered from failure with oedema the G.F.R. was still significantly reduced.

In 46 of the 60 cases additional information was obtained by cardiac catheterization—performed simultaneously with the renal measurements in half of them. An estimate could thus be made of the proportion of the cardiac output going to the kidneys, which was much the same in Groups I, II, and III, showing a fairly wide variation between about 12 and 30%. In Groups IV and V, however, the proportion was lower and relatively constant, being between 10 and 15%. This the authors attribute in part to the low value and fixity of the cardiac output in congestive failure. Renal blood flow was noted to be low when the oxygen content of mixed venous blood was low and the arteriovenous oxygen difference high, and vice versa. The renal blood flow was related to venous pressure only in those cases in which the latter was considerably increased (above 10 cm. of water), the renal blood flow being reduced in all such cases. *J. A. Cosh*

679. **The Hemodynamic Alterations Produced by a Plastic Valvular Prosthesis for Severe Aortic Insufficiency in Man**

J. C. ROSE, C. A. HUFNAGEL, E. D. FREIS, W. P. HARVEY, and E. A. PARTENOPE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 891–900, June, 1954. 6 figs., 11 refs.

At Georgetown University Hospital and the Veterans Administration Hospital, Washington, D.C., the authors have studied the circulatory dynamics in 9 patients with severe aortic insufficiency before and after the insertion of a plastic ball valve in the descending aorta below the origin of the subclavian arteries by Hufnagel's technique (*Bull. Georgetown Univ. med. Cent.*, 1951, **4**, 128). Precise details of all the methods of investigation are given; they included the use of dye concentration curves.

It was found that while there was ample evidence from pressure pulse tracings taken from the femoral artery that the valve was effective in reducing regurgitation, tracings from the brachial artery showed a fall in diastolic pressure and an increase in pulse pressure. Cardiac output was increased in 6 cases, probably owing to an increase in the efficiency of ventricular contraction and to more complete emptying at each systole as well as to an absolute reduction in the volume of regurgitation, since improvement was seen in dye concentration curves obtained not only from the femoral artery but also from the brachial artery, in which regurgitation still occurred after operation. *J. R. Belcher*

680. **Selection of Patients for Mitral Commissurotomy in Relation to Clinical Results**

O. C. JULIAN, W. S. DYE, and W. J. GROVE. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **69**, 273–281, Sept., 1954. 8 refs.

The authors first point out that the degree of damage to the valve in cases of mitral disease is not the only factor to be taken into consideration in assessing the value of valvotomy in any particular case, and stress the importance of the state of the myocardium. In this paper they present a pre- and post-operative evaluation in 139 cases in which commissurotomy was performed, the follow-up period being more than a year in 65 cases. There were 7 postoperative deaths, and the late mortality (17 deaths) was relatively high, particularly in patients with severe disability. The results were poor in a high proportion of the patients with left ventricular enlargement (21 out of 35). The late follow-up results were based on the patient's own assessment, being "good" or "excellent" in 65 and "worse" in only 4. Embolism occurred in 9 cases in the series, and was fatal in 4.

The authors state that although the mortality in patients in Grade IV (classification of the New York Heart Association) was very high (19 out of 39) the operation is nevertheless justified as the results in the survivors were good. *J. R. Belcher*

681. **Calcification of the Mitral Valve Annulus and Its Relation to Functional Valvular Disturbance**
M. A. SIMON and S. F. LIU. *American Heart Journal* [*Amer. Heart J.*] **48**, 497–505, Oct., 1954. 3 figs., 18 refs.

Calcification of the mitral valve annulus is not infrequent. Its incidence was 10% in 590 unselected, consecutive autopsies on subjects of all ages. The incidence was higher in individuals over 50 years of age.

While calcification of the annulus of the mitral valve may occur in rheumatic heart disease, it is primarily a degenerative process similar, in many respects, to arteriosclerosis. In the majority of cases the process does not affect the mitral valve leaflets. Variable degrees of calcification of the aortic valve, presumably on a non-rheumatic basis, were associated in approximately 25% of the subjects whose hearts showed calcification of the mitral valve annulus.

In a selected series of 24 cases of mitral annulus calcification, apical systolic murmurs presumably referable to the mitral valve, were heard in 15 cases. In 9 of these 15 cases the quality of the murmurs was such (loud, rough, or musical) as may be associated with functional derangement at the mitral orifice, and in 5 instances a clinical diagnosis of mitral regurgitation was made.

In the light of our newer knowledge of the mechanics of the closure of the mitral valve, it is suggested that extensive calcification of the mitral valve annulus interferes with the rhythmic muscular contraction of the mitral ring by forming a rigid, non-compressible segment of that ring. Thus, the gap to be bridged may not be sufficiently reduced to permit the overlapping closure by the mitral leaflets. This concept of interference with contraction of the valve ring, together with the observation that 60% of apical systolic murmurs in our proved cases of mitral annulus calcification have special qualities suggesting mitral dysfunction, is construed as presumptive evidence that extensive mitral annulus calcification (without rheumatic involvement of the leaflets) may produce relative or frank mitral regurgitation. Whether such mitral regurgitation, either relative or frank, as may be produced by mitral annulus calcification is sufficient to further impair the cardiac function of subjects in an older age group, the majority of whose hearts are already partially damaged, is extremely difficult to assess.

Extensive calcification of the mitral valve annulus which may produce variable degrees of mitral regurgitation can be strongly suspected in individuals over 50 years of age having loud, rough, or musical systolic apical murmurs who give no history of previous rheumatic heart disease.—[From the authors' summary.]

682. **Biopsies of the Lung and Atrial Appendages in Mitral Stenosis: Correlation of Data from Cardiac Catheterization with Pulmonary Vascular Lesions**
J. DENST, A. EDWARDS, K. T. NEUBUERGER, and S. G. BLOUNT. *American Heart Journal* [*Amer. Heart J.*] **48**, 506–520, Oct., 1954. 9 figs., 30 refs.

Lung biopsies from 23 patients with mitral stenosis who were studied by cardiac catheterization prior to mitral commissurotomy were examined histologically. In the majority of cases the muscular arteries and arterioles exhibited prominent fibroelastic intimal thickening, and in 32% the media appeared hypertrophic. In general, a positive correlation existed between the degree of vascular alteration and the pulmonary arteriolar resistance and mean pulmonary arterial pressure in the more severe cases of pulmonary hypertension. The hemodynamic pattern varied considerably in patients who exhibited less severe vascular lesions. A functional component was believed to be of as great importance in the development and maintenance of pulmonary hypertension as the organic vascular changes. It was considered that surgery should not be denied the patient either on the basis of data obtained by cardiac catheterization or because of the pulmonary vascular lesions, which are not usually severely obstructive although almost always present.

The histologic findings in 75 resected atrial appendages were reviewed; the results were in general agreement with those of other recent investigations.—[Authors' summary.]

683. **The Nature of Pulmonary Hypertension in Mitral Stenosis**
L. G. DAVIES, J. F. GOODWIN, and B. D. VAN LEUVEN. *British Heart Journal* [*Brit. Heart J.*] **16**, 440–446, Oct., 1954. 4 figs., 24 refs.

The effect of hexamethonium bromide on the pulmonary circulation of 12 patients with mitral valvular disease was studied during cardiac catheterization at the Postgraduate Medical School of London. The cardiac output and pulmonary and systemic arterial pressures were measured before and after the administration of hexamethonium, which was injected down the catheter in doses of 15 to 20 mg.

In the 4 cases in which the pulmonary systolic pressure was between 55 and 90 mm. Hg hexamethonium produced a maximum fall in pulmonary systolic pressure of 30 to 40% of the resting value. The fall in systemic pressure was much less, and the cardiac output remained unchanged. In the other 8 cases, in which the pulmonary pressure was normal or only moderately raised, the drug caused no significant change in pressure or cardiac output. The authors conclude that the fall in pulmonary systolic pressure without fall in cardiac output produced by hexamethonium in patients with severe and moderately severe pulmonary hypertension indicates a reduction in pulmonary vascular resistance, perhaps resulting from pulmonary arteriolar dilatation.

The relationship between paroxysmal dyspnoea and severe pulmonary hypertension was examined in 103 cases of mitral disease. The resting pulmonary arterial pressure was measured in 51 of these patients, 22 of whom had a history of attacks of spontaneous dyspnoea or orthopnoea; in 13 of these 22, and in only 7 of the remaining 29, the pulmonary systolic pressure was above 60 mm. Hg. In the same 51 patients and in 52 others an estimate of the pulmonary arterial pressure was made by examination of the radiological appearances. A significant correlation was found between the occurrence of paroxysmal dyspnoea and the presence of evidence of severe pulmonary hypertension.

The authors conclude that severe pulmonary hypertension is associated with attacks of dyspnoea and that the absence of any untoward symptoms on reducing pulmonary arterial pressure with hexamethonium suggests that the increase in pulmonary arteriolar resistance may not be "protective" as has been thought. They consider that hexamethonium may be of value in the treatment of patients with mitral stenosis and severe pulmonary hypertension who are unsuitable for valvotomy (for example, those with predominant mitral incompetence), and of attacks of paroxysmal dyspnoea in such cases. *D. Emslie-Smith*

HEART FAILURE

684. **The Right Atrial Pulse in Congestive Heart Failure**
P. KORNER and J. SHILLINGFORD. *British Heart Journal* [*Brit. Heart J.*] **16**, 447–450, Oct., 1954. 4 figs., 3 refs.

The authors analyse records of the right atrial pressure pulse obtained by cardiac catheterization and strain-gauge manometry during quiet respiration from 48 patients studied at the Postgraduate Medical School of London, 44 of whom had heart disease of various types. The normal right atrial pressure curve shows a positive wave ("a"), with atrial systole, followed by a negative wave ("X") (corresponding to atrial diastole and the descent of the base of the heart); a second positive wave ("v") due to passive atrial filling then occurs and is followed by a negative wave ("Y") to complete the cycle, X being usually deeper than Y. In atrial fibrillation with a normal venous pressure a is absent and X and Y are often fused.

Irrespective of heart rate or rhythm or of the type of cardiac disease present, a raised venous pressure is always accompanied by changes in the atrial pressure pulse. As the mean atrial pressure rises above about 5 mm. Hg (referable to 5 cm. below the sternal angle) the depth of the X wave progressively lessens until at a mean pressure of about 10 mm. Hg a positive wave appears instead. There is a corresponding, but slower, rise in the level of Y.

The positive systolic wave which replaces X is associated with tricuspid regurgitation. The authors suggest that a diminution in depth of X indicates a small tricuspid leak, and that these changes demonstrate an association between raised venous pressure and tricuspid insufficiency without indicating which factor is causal.
D. Emslie-Smith

685. **Red Half-moons in Cardiac Failure**
R. TERRY. *Lancet* [*Lancet*] **2**, 842–844, Oct. 23, 1954. 2 figs., 4 refs.

The author has observed red suffusion of the half-moons at the base of the finger nails (usually best seen in the thumb nail) in 23 patients (3 female, 20 male), the youngest being aged 40, of whom 14 had congestive heart failure, 4 advanced pulmonary disease with dyspnoea, and the remainder systemic conditions, such as polycythaemia vera and Hodgkin's disease, or diseases with systemic effects, such as cirrhosis of the liver. Congestive heart failure therefore predominated. The phenomenon has not been observed in patients with local conditions such as peptic ulcer and hernia, nor was it found in a group of 150 healthy young women, and its occurrence may therefore be of some clinical significance.

Examination of the under-surface of the dried, excised, normal nail shows that a membrane, the superficial layer of the nail-bed, is attached firmly to the distal part of the nail, but only loosely in the region of the half-moon, and the author suggests that a red half-moon is caused by the nail-bed in the region of the half-moon becoming adherent to the nail. However, he has not yet had an opportunity of examining the excised nail of a patient with red half-moons. *Arthur Willcox*

686. **Studies on the Excretion of Chloride by Man with and without Congestive Heart Failure, Using Long-life Radiochloride Cl^{36}**
C. T. RAY, S. A. THREEFOOT, and G. E. BURCH. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 663–701, Nov., 1954. 17 figs., 17 refs.

CONGENITAL HEART DISEASE

687. **Closure of Atrial Septal Defects**
E. HUSFELDT and H. R. SØRENSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 93–94, Aug., 1954. 4 refs.

Closure of an atrial septal defect was attempted in 12 cases at Rigshospitalet, Copenhagen, by an antero-posterior suturing technique aided by a finger introduced through the right auricular appendage. The defect was closed in 4 cases and reduced to negligible proportions in 6, and there were 2 postoperative deaths.
S. F. Stephenson

688. **Causative Factors Underlying Congenital Heart Malformations. I. Patent Ductus Arteriosus**
R. C. ANDERSON. *Pediatrics* [*Pediatrics*] **14**, 143–152, Aug., 1954. 15 refs.

In a study of the factors leading to congenital malformations of the heart the case histories and family histories of 205 patients (54 males and 151 females) who had had operations for patent ductus arteriosus at the University Hospital, Minneapolis, Minnesota, were investigated. Information was collected by written questionary about the first-degree relatives of 117 of these 205 patients. Four of the patients were excluded from the survey because of a maternal history of rubella, and another 8 because of the presence of additional cardiac defects. It was found that 2 of the 145 later-born siblings of the 105 remaining patients also had patent ductus arteriosus, and one of these had had coarctation of the aorta as well; no non-cardiac congenital defects were reported in this group. None of the 210 parents or of the 28 children of the patients had congenital heart defects, and none of the patients had been born of consanguineous marriages. Four of them were members of probable monozygous twin pairs, but in none of these cases was the second twin affected.

No effect of birth order on the incidence of patent ductus arteriosus was apparent in the 63 families considered under this head.

The general incidence of patent ductus arteriosus in Minnesota is estimated to lie between 1 in 2,500 and 1 in 5,000 births, and it is concluded that there is a definite familial concentration of this anomaly.

C. O. Carter

689. **The Left-sided Superior Vena Cava**
M. CAMPBELL and D. C. DEUCHAR. *British Heart Journal* [*Brit. Heart J.*] 16, 423–439, Oct., 1954. 13 figs., 37 refs.

The early embryonic great veins are bilaterally symmetrical. Later they become unilateral and asymmetrical, the left anterior cardinal vein becoming occluded proximal to the branch communicating with the corresponding vein on the right side, and this communicating branch becoming the left innominate vein. If the left anterior cardinal vein persists, it becomes a left-sided superior vena cava (S.V.C.) draining through the coronary sinus into the right atrium. Out of a series of more than 1,500 cases of congenital heart disease seen at Guy's Hospital, London, a persistent left S.V.C. occurred in 46 (3%), being present in over 40% of cases of dextrocardia and isolated laevocardia, but in only 2% of other cases. In at least 30 of the 46 a normal right S.V.C. was also present.

Of the 28 patients in whom there was no transposition of the heart or viscera, 21 had cyanotic heart disease, 14 of these having Fallot's tetralogy. Of the 7 acyanotic cases, 3 had simple pulmonary valvular stenosis with left-to-right shunt and 4 had atrial septal defects. Of the remaining 18 patients, 6 had isolated laevocardia with a left-sided venous atrium, 4 had dextrocardia (with transposition of the venous atrium in one case) and transposition of the viscera, 3 had isolated laevocardia with a right-sided venous atrium, and 5 had dextrocardia without transposition of the viscera. In the 7 cases of transposition of the venous atrium the left S.V.C. seemed to be the only one; it emptied directly into the venous atrium, the pulmonary veins emptying into a right arterial atrium. A lone left S.V.C. is found only in this condition and in complete situs inversus. In 34 of the other 39 cases, in which both right and left S.V.C. were generally present, the left one seemed to drain into the right atrium or into the right side of a single atrium; in the remaining 5 cases it drained into the left side of a single, or virtually single, atrium. A left S.V.C. draining into a normal left atrium was not seen in any case. In 4 cases of left S.V.C. with complex defects there was no true inferior vena cava, the blood returning to the heart through a large azygos vein.

The presence of a persistent left S.V.C. gives no clinical signs, though a broad, straight-edged vascular pedicle may be seen on radiography, and it can usually be demonstrated by cardiac catheterization and angiocardiography from the left arm. It does not appear to be of any practical importance, though it may make cardiac catheterization from the left arm somewhat difficult.

D. Emslie-Smith

BLOOD VESSELS

690. **The Action of Anticoagulants and of Lipocaic Hormone in Atherosclerosis.** (Action des anticoagulants et de l'hormone lipocaïque sur l'équilibre humoral des athéroscléreux)
R. RAYNAUD, J. ROBERT D'ESHOUGUES, and P. PASQUET. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] 47, 426–432, May, 1954.

Working at the University of Algiers the authors have previously shown by paper electrophoresis that an abnormal pattern of the serum lipoproteins occurs in the stage of evolution of atherosclerosis, consisting in an increase in the large-molecule lipoproteins designated "β slow" and "β very slow", with a corresponding diminution of the small-molecule fraction referred to as "α very slow". In 8 out of 10 atherosclerotic patients in the present study who were given intermittent heparin therapy (100 mg. intramuscularly or intravenously three times weekly for 3 to 5 weeks) the serum lipoprotein pattern was restored to normal. Similar results were obtained in a further 9 patients who received continuous treatment with "tromexan" (ethyl biscoumacetate).

Although both drugs favourably affected the coagulability of the blood, there was no relation between this effect and the alteration of the lipoprotein pattern. Heparin caused clinical improvement in the patients with angina of effort, but this improvement also was unrelated to the effect on the serum lipoproteins. In a further study lipocaic hormone ("lipormone") was administered to 6 patients with atherosclerosis, arteritis, or angina in a dose of 0·6 g. daily for 2 to 4 weeks. There was an increase in the level of lipoproteins of Group α (Fraction A plus Fraction α rapid) in all 6 cases and a conversion of β slow to β rapid lipoproteins in 2 cases, although the latter effect is not attributed by the authors to the action of the drug [on not very convincing grounds]. The authors conclude by recommending that atherosclerosis should be treated with tromexan supplemented by lipocaic.

[The case summaries given in the tables do not always agree with the details given in the text. Also, it is not clear for what type of case this treatment is recommended. The results are of considerable theoretical interest, but the authors do not provide enough evidence to show that the correction of the abnormal lipoprotein pattern achieved by the use of tromexan and lipocaic is of sufficient importance to justify the clinical use of these drugs for this purpose.]

Bernard Isaacs

691. **Peripheral Neuropathy in Periarteritis Nodosa**
K. W. G. HEATHFIELD and J. R. B. WILLIAMS. *Lancet* [*Lancet*] 2, 673–677, Oct. 2, 1954. 4 figs., 7 refs.

The authors describe one case of mononeuritis multiplex and 8 cases of symmetrical neuropathy due to periarteritis nodosa seen in a practice covering four general hospitals in London. They note that the former condition is characteristic of periarteritis nodosa, while the latter is clinically indistinguishable from the symmetrical neuropathy which occurs in diabetes, acute infective

polyneuritis, bronchogenic carcinoma, alcoholism, vitamin-B deficiency, pulmonary tuberculosis, and chronic progressive polyneuritis.

All the patients with symmetrical neuropathy had similar symptoms. There was shooting and burning pain in the legs, worse at night. Later, distal paralysis occurred, the extensor muscles being more affected than the flexor group. Muscle wasting, tenderness in the calf, and loss of vibration and position sense followed. The ankle-jerks were commonly absent, but the knee-jerks were retained. The arms became involved in 3 cases. Distinguishing features in this type of case are listed as: raised erythrocyte sedimentation rate, raised serum globulin level (shown by electrophoresis to be chiefly gamma globulin), and normochromic anaemia with a leucocytosis and a tendency to eosinophilia; the urine commonly contains protein, blood cells, and casts, and the blood urea level is raised. Cutaneous or subcutaneous nodules were found to be inconstant. At necropsy there was macroscopic evidence of arterial disease affecting heart, liver, kidneys, and intestinal tract. The most difficult differential diagnosis is from bronchogenic carcinoma, since, as the authors point out, a normal chest radiograph does not exclude such a diagnosis.

[This is a valuable paper which should be read in full, as the case notes are instructive.] *Geoffrey McComas*

692. **Veins after Sympathectomy**

P. BEACONSFIELD. *Surgery* [*Surgery*] **36**, 771–776, Oct., 1954. 2 figs., 8 refs.

The author, working at the Postgraduate Medical School of London, has studied the rate of regain of tone in the veins of 4 patients after sympathectomy. The state of the superficial veins in the forearms was recorded by infra-red photography at intervals up to one year after the performance of cervicodorsal sympathectomy, and the blood flow in the forearm and hand and the hand volume were recorded at the same intervals. Indirect heating tests to assess the completeness of sympathectomy were also carried out, and showed some return of autonomic reflex activity at the end of a year.

Blood flow in the hand and forearm and hand volume increased after sympathectomy, and the infra-red photographs showed the superficial veins to be dilated. Three months later blood flow had returned to the preoperative level, but the hand volume was still increased. One year after sympathectomy the hand volume had also returned to the preoperative figure, but the forearm veins still appeared to be dilated. Attempts to study the veins of the foot by infra-red photography were not successful, but measurement of the blood flow and volume of the foot for a year after sympathectomy in 6 subjects gave results which varied little from those obtained for the hand.

The author concludes that after an initial dilatation, as evidenced by the photographs and increased limb volumes, regain of tone soon begins in the veins, as in the arteries, after sympathectomy. It proceeds more slowly than in the arteries, taking at least a year to complete compared with 3 months or less for arteries. It is suggested that the elevated skin temperature found in sympathectomized limbs after the blood flow has returned to the preoperative level may be in part the result of the persisting diminution of tone in the veins [but it is not made clear how an increase in the volume of blood in the veins, the consequence of their reduced tone, without an increase in its rate of flow, can influence skin temperature]. *C. J. Longland*

SYSTEMIC CIRCULATORY DISORDERS

693. **Comparison of Indirect and Direct Methods of Measuring Arterial Blood Pressure**

F. H. VAN BERGEN, D. S. WEATHERHEAD, A. E. TRELOAR, A. B. DOBKIN, and J. J. BUCKLEY. *Circulation* [*Circulation* (*N.Y.*)] **10**, 481–490, Oct., 1954. 18 figs., 11 refs.

In this paper from the University of Minnesota the authors show that there is frequently a discrepancy between the results of direct and indirect determinations of blood pressure, which is particularly noticeable in patients in surgical shock. In 65 out of 70 surgical patients studied in the immediate postoperative period from 2 to 14 direct and indirect readings were obtained, each direct reading being taken as soon as possible after the associated indirect reading. Direct measurements were made by means of a strain gauge and an indwelling brachial arterial needle. Indirect measurements were by auscultatory, palpatory, and oscillometric methods.

It was found that indirect measurements consistently fell below the direct readings, this discrepancy increasing with higher blood pressures and being greatest in young hypertensive patients and in thin subjects. The descending order of accuracy for the indirect methods was: oscillometric, auscultatory, and palpatory, but the differences between these results were relatively small. The significance of these findings in the young hypertensive subject is discussed. It is pointed out that no criticism is made of readings obtained by indirect methods provided these are regarded mainly as indices of the true values obtaining intra-arterially.

The authors suggest that the discrepancies described may be due to the effect of the summation of the peripherally reflected pulse waves upon the central wave, this resulting in a peripheral intra-arterial reading higher than that obtained by the auscultatory method. It is possible therefore that the auscultatory method measures the central aortic pressure and not the peripheral pressure in the artery at the site of measurement. The appearance of the Korotkoff first sound is mainly caused by the pressure of the central wave. They found the muffling of the Korotkoff sounds to correspond more closely to the intra-arterial diastolic pressure than did their disappearance. *J. Warwick Buckler*

694. **Sodium Output–Blood Pressure Relationships and Their Modification by Treatment**

D. M. GREEN and E. J. ELLIS. *Circulation* [*Circulation* (*N.Y.*)] **10**, 536–543, Oct., 1954. 5 figs., 6 refs.

Working at the University of Southern California School of Medicine, Los Angeles, the authors have studied the urinary sodium excretion, expressed as mEq.

per sq. metre of body surface area per minute, in 50 hypertensive and 25 normotensive subjects on self-selected fluid and dietary intakes. Water output was expressed in ml. per sq. metre per minute. Urinary sodium excretion was determined (*a*) under basal conditions, (*b*) over 24-hour periods, and (*c*) after loading with 100 ml. of 5% saline per sq. metre body surface, and with mannitol in an initial dose of 8 g. per sq. metre followed by sustaining doses of 75 mg. per sq. metre per minute. Blood-pressure readings were taken every 20 minutes during the periods of urine collection, the mean pressure being calculated as half the sum of the systolic and diastolic pressures. In 26 subjects the output under load was also studied after various forms of medical and surgical therapy.

From this study the authors draw the following conclusions: (1) The urinary excretion of sodium by hypertensive patients is significantly higher than in normotensive subjects; this applies to the 24-hour output, basal output, and output under load. (2) This higher output is due to an increased appetite for sodium among hypertensive subjects. (3) Although there are considerable variations, in general the level of sodium excretion tends to parallel the level of the blood pressure. (4) When the blood pressure of hypertensive patients is reduced by therapy, the urinary output of sodium under load is also reduced. *J. Warwick Buckler*

695. **Volume of the Fluid Compartments in Human and Experimental Hypertension**

H. C. TENG, A. P. SHAPIRO, and A. GROLLMAN. *Metabolism* [*Metabolism*] **3**, 405–411, Sept., 1954. 12 refs.

The plasma volume, extracellular fluid volume and total body water of a group of normotensive subjects and a group of hypertensive patients of nearly similar body build were studied. There was an appreciable expansion of extracellular fluid volume in patients with essential hypertension together with a suggested increase in total body water. Significant increases in total body water were observed in dogs after induction of hypertension. This evidence further supports the concept of a defect in water and electrolyte metabolism in hypertensive vascular disease.—[Authors' summary.]

696. **Rauwolfia Serpentina in Hypertensive Vascular Disease**

G. A. PERERA. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 453–456, July, 1954. 1 fig., 4 refs.

The author describes the effect of "raudixin" (a preparation of rauwolfia serpentina) in doses of 50 to 100 mg. twice daily on the blood pressure and heart rate in 10 ambulatory cases of uncomplicated hypertension treated at the Presbyterian Hospital (Columbia University), New York. They were treated for one month, the blood pressure having been recorded at weekly intervals for at least a month before treatment. Raudixin was also given in a dose of 100 mg. twice a day for 2 to 4 weeks to 10 in-patients in the "accelerated" (malignant) phase of hypertension (diastolic pressure over 120 mm. Hg), while a third group of 4 hypertensive patients with or without cerebral or renal complications underwent more detailed metabolic and haemodynamic studies during the administration of 100 to 200 mg. twice daily for 15 to 25 days.

The drug had a significant depressor effect (more than 15 mm. Hg systolic and 10 mm. Hg diastolic) on 7 out of the 10 patients in the ambulatory group, and emotionally tense patients in this group were noted to be more relaxed, but it had little effect on the patients in the second group. Temporary sodium retention was the only metabolic effect noted in the third group, while the plasma volume, splanchnic blood volume, and cardiac output were unaffected. *G. S. Crockett*

697. **Comparison of Effects on Hypertension of Hexamethonium and Pentapyrrolidinium Injected Subcutaneously**

N. C. BIRKHEAD and E. V. ALLEN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 489–496, Sept. 1, 1954. 2 figs., 9 refs.

The duration of the hypotensive effect of a test dose of pentapyrrolidinium bitartrate ("ansolysen") was determined at the Mayo Clinic on 12 patients with hypertension and compared with that of a comparable dose of hexamethonium chloride in order to test the claim that ansolysen has a more prolonged action. Both drugs were given subcutaneously, the dose of ansolysen being 3 mg. and that of hexamethonium 10 mg., and the blood pressure was determined after the injection at 10-minute intervals with the patient lying, sitting, and standing.

In 5 cases the effect of ansolysen lasted longer than that of hexamethonium; in 4 each drug reduced the blood pressure for approximately the same length of time; and in 3 hexamethonium produced a more prolonged effect on readings taken in the sitting and standing positions only.

[This work would not seem to have much bearing on the practical treatment of hypertension, since ansolysen is essentially intended to be given by the mouth.]

C. W. C. Bain

698. **Pentapyrrolidinium Bitartrate (M. & B. 2050A) in the Treatment of Hypertension: Preliminary Observations**

R. W. GIFFORD, E. V. ALLEN, and N. C. BIRKHEAD. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 496–508, Sept. 1, 1954. 6 refs.

"Ansolysen" (pentapyrrolidinium bitartrate) was given by mouth to 12 patients with hypertension over a period of one month or more and to one patient subcutaneously for 6 months. The drug was also given for shorter periods (3 days to 3 weeks) by mouth or subcutaneously to 11 other patients with hypertension. Rauwolfia serpentina or other adjuvant drugs were given in only a few of the cases: consequently the dosage of ansolysen was high, reaching 300 mg. daily in some cases, and complications tended to be severe. Constipation, dizziness on standing, and dryness of the mouth were the most frequent; retention of urine occurred twice, and paralytic ileus once. The authors therefore conclude

that " the use of pentapyrrolidinium should be restricted to patients with severe hypertension that has failed to respond to simpler treatment and should be initiated only for hospitalized patients by physicians familiar with the capriciousness of ganglionic blocking agents ".

[The validity of conclusions drawn from so small a series treated over so short a period is questionable, and readers in Great Britain, where there must be many clinics with experience of hundreds of cases treated with ansolysen, will learn little from this trial. The high incidence of side-effects is not surprising in view of the large doses of ansolysen which the authors were forced to use when the drug was given alone.]

C. W. C. Bain

699. **Treatment of Hypertensive Disease by Drug-induced Sleep.** (О лечении больных гипертонической болезнью медикаментозным сном)
N. A. Kevdin, R. F. Zubova, and V. N. Zakharchuk. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **32**, 62–70, Sept., 1954. 11 refs.

Following Pavlov's teaching on the value of sleep in protecting the sensory cells of the cerebral cortex from overstimulation and exhaustion and in restoring their normal function, the authors have employed sleep therapy in the treatment of cases of psychosis (especially schizophrenia), neurosis, and also of hypertension.

Sleep may be induced by hypnosis, rhythmic galvanic current applied to the head, ultraviolet irradiation of the soles of the feet, short-wave diathermy of the abdomen, or by hypnotic drugs. The last-named method is the simplest and is usually effective, but if prolonged is liable to produce toxic effects, including disturbances in the cardiovascular, respiratory, and vegetative nervous systems, although these effects can be minimized by careful selection of cases, and by limiting the courses of drug treatment to 7 days, with intervals of 5 days between each course. Proper preparation of the patient and the provision of suitable surroundings enable the desired effect to be obtained with lower doses of hypnotics; isolated sound-proof rooms with shaded lights are preferable to large general wards. The patients are allowed to wake up spontaneously and are not aroused; when they awake, they are taken to a lighted ward or dining room for breakfast or dinner, and after dinner take a little exercise before returning to their rooms for further sleep. Sleep should be maintained for 16 to 20 hours out of the 24, and should be neither too deep nor too light. The authors' usual method is to give a 5- or 6-day course of bromides (9 grains (0·6 g.) of sodium bromide 3 or 4 times daily), followed by a course of 3 grains (0·2 g.) of barbitone sodium or amylobarbitone sodium 3 times a day or, in the absence of cardiovascular disease, an enema of 15 to 20 grains (1 to 1·3 g.) of chloral hydrate. The exact dosage is determined in each case after careful clinical investigation.

Among the patients treated were 125 with hypertension —31 men and 94 women, of whom 90 were between the ages of 50 and 70. In 67 cases the results were good, a steady and well-marked decline in arterial pressure taking place. In 36 cases only a slight fall in pressure resulted, while in 8 cases treatment had to be curtailed owing to myocardial failure (2 cases), emphysema following hypostatic pneumonia (2), or toxicosis (4). The authors emphasize that drug-induced sleep should be undertaken with caution in elderly patients with established vascular sclerosis or cor pulmonale, and is definitely contraindicated for patients with severe general or cerebral atherosclerosis, or renal or hepatic insufficiency. It is important after conclusion of the treatment to ensure that the patient returns to conditions of life and work in which factors disturbing to the mind are reduced to a minimum.

[This article gives a well-balanced account of a method widely practised in the U.S.S.R. for the treatment of a number of diseases associated with mental stress, including peptic ulceration.] *L. Firman-Edwards*

PULMONARY CIRCULATION

700. **Primary Pulmonary Hypertension. A Report of Three Cases**
A. W. Branwood. *Edinburgh Medical Journal* [*Edinb. med. J.*] **61**, 332–341, Oct., 1954. 12 figs., 12 refs.

The clinical and pathological features of 3 cases of primary pulmonary hypertension are described in this paper from the University of Edinburgh. The patients were women, aged 38, 37, and 22 years respectively, and in all 3 cases the main clinical features of primary pulmonary hypertension were present—namely, severe breathlessness and cyanosis increasing on exercise, oedema of the legs, and right ventricular enlargement. No cause for the pulmonary hypertension could be found. Two of the patients had attacks of syncope and one had cardiac pain, but none had moist sounds in the chest. All 3 patients died suddenly a short time after admission to hospital, the disease being rapidly progressive once symptoms developed. One patient did not benefit from administration of digoxin intravenously and died a short time after the injection.

At necropsy there was chronic venous congestion in all organs but no evidence of arterial disease except in the pulmonary vessels. Right ventricular hypertrophy was present and there was dilatation of the pulmonary vessels with atheroma of the intima, but no medial or adventitial change. In the arterioles gross intimal thickening, often reducing the lumen to a slit, was observed. Some round cells were present in the intima. The internal elastic lamina was split and reduplicated. The media showed pressure atrophy in areas beneath the greatly thickened intima, but the adventitia was normal. Alveolar capillaries and lungs were normal.

The author points out the similarity between essential hypertension and primary pulmonary hypertension, the causes of which are unknown. He suggests that the increased pulmonary pressure is brought about by the increased tone of the vessels, and that since improvement sometimes follows administration of " priscoline " (benzazoline) the autonomic nervous system may be involved. *A. Gordon Beckett*

Haematology

701. The Natural History and Management of Haemolytic Transfusion Reactions

G. DISCOMBE. *Lancet* [*Lancet*] **2**, 936–939, Nov. 6, 1954. 45 refs.

The author adds 3 more cases of haemolytic transfusion reaction to the 11 cases he described previously (*Lancet*, 1952, **1**, 734), and reviews all 14 together. In 3 cases there was no discoverable cause, in 4 the reaction was due to an administrative mistake, in 6 it was due to laboratory or technical error, and in one it was apparently due to donor antibodies. The 10 recipients who had received incompatible blood showed mild symptoms only; in 9 out of the 10 ABO incompatibilities were present, and the recipient had received 150 ml. or more of incompatible blood; the tenth was a case of rhesus incompatibility. On the other hand the 3 patients in whom no serological error could be detected all had severe symptoms, and one died. The symptoms of the mild haemolytic transfusion reaction—simple rigor, fever, and lumbar pain with haemoglobinuria—differ from those of the fatal reaction, in which the patient develops severe hypotension, possibly with respiratory distress, diarrhoea, and convulsive attacks.

The author discusses the question whether fatal transfusion reactions are caused by some allergic response independent of the relatively benign haemolysis. "Were the hypothesis of an allergic reaction to be accepted, one would expect that intravascular haemolysis of a patient's own blood would rarely, if ever, cause the symptoms seen in incompatible transfusions, but that heterologous blood, or autogenous blood modified by some foreign haptene, might do so. This is, in fact the case." Such allergic responses might be based on some antigen–antibody reaction outside the blood-group system, or caused by some constituent of the plasma. [It would be of interest to know whether the 3 patients who died had a previous history of allergic reactions.]

The treatment advised is to restore the systolic and diastolic blood pressure by means of vasoconstrictors acting directly on the vessel wall, such as noradrenaline and methylamphetamine hydrochloride. In addition it may be profitable to give antihistamine drugs. The infusion of sodium sulphate and sodium lactate solutions is contraindicated. Anuria should be treated by the Bull–Borst method (*Lancet*, 1949, **2**, 229; *Abstracts of World Medicine*, 1950, **7**, 304). The author deprecates any attempt on the part of hospital authorities to lay down rules and regulations "to prevent the doctors from making any mistakes" in blood transfusion. Such rules usually make no provision for the desperate emergency. The author emphasizes that "no consultant should accept such instructions unless he knows who was the expert, or the group of experts, who drew up those instructions, and unless he has the opportunity of discussing the matter with that expert, should he so desire".

Kate Maunsell

702. Congenital Afibrinogenemia. A Study of Some Basic Aspects of Coagulation

B. ALEXANDER, R. GOLDSTEIN, L. RICH, A. G. LE BOLLOC'H, L. K. DIAMOND, and W. BORGES. *Blood* [*Blood*] **9**, 843–865, Sept., 1954. 9 figs., 48 refs.

In a study at the Beth Israel Hospital and Children's Medical Center (Harvard Medical School), Boston, of 3 subjects with congenital afibrinogenaemia, the opportunity was taken to investigate further the changes which occur in blood in the process of coagulation independently of the thrombin–fibrinogen–fibrin interaction. The blood of these subjects was incoagulable and contained no more than about 1 mg. of fibrinogen or fibrinogen-like substance per 100 ml.

It was found that shortly after the blood was exposed to glass there was progressive agglutination and lysis of platelets and that plasma antihaemophilic activity, originally normal, declined rapidly and practically disappeared. Factor V was rapidly consumed and Factor VII (S.P.C.A.) appeared in a normal manner. These changes were well established before consumption of prothrombin could be detected, the latter occurring at a normal or slightly increased rate.

It was observed also that thrombin added to the fibrinogen-free plasma induced platelet agglutination: this did not occur when thrombin was added to platelets alone. The natural antithrombic activity of the plasma was found to be normal and the heparin cofactor was present.

Experiments relating the one-stage prothrombin time to the fibrinogen concentration revealed that if the prothrombin time of a plasma is normal, the fibrinogen content of the plasma must be over 100 mg. per 100 ml. Below this level the prothrombin time rises progressively, and if the fibrinogen level is such that the prothrombin time is very prolonged, orthodox methods of plasma fibrinogen determination may be unreliable.

A. Brown

ANAEMIA

703. The Simultaneous Occurrence of Benign Thymoma and Refractory Anemia

J. F. ROSS, S. C. FINCH, R. B. STREET, and J. W. STRIEDER. *Blood* [*Blood*] **9**, 935–952, Oct., 1954. 12 figs., 30 refs.

The simultaneous occurrence in each of 2 cases of a benign thymoma and a severe anaemia which failed to respond to all known haematopoietic agents and also to ACTH and cortisone is reported in this paper from the Massachusetts Memorial Hospitals, Boston. In both cases the anaemia was unaffected by removal of the thymoma and was controlled only by repeated blood transfusion. Bone-marrow biopsy revealed hypoplasia of the erythropoietic elements with active granulopoiesis. Histological examination showed both the tumours

to be composed of two types of cell—a cell identical with the adult lymphocyte, generally occurring in uniform sheets, and a spindle cell occurring in interlacing whorls and tending to "pseudorosette" formation. Reference is made to 7 similar cases reported in the literature.

The authors point out that the chance occurrence of these two rare conditions in the same individual is statistically improbable. The contention that the thymoma causes the anaemia rather than the reverse is supported by the fact that in the first case the tumour had been present for 3 years before the anaemia developed. The authors conclude that, whatever the aetiology, these disorders are related and they recommend careful study of the thymus and the bone marrow whenever a case of either thymoma or refractory anaemia is encountered. *E. G. Rees*

704. **Pure Red-cell Anaemia in Patients with Thymic Tumours**

J. N. M. CHALMERS and K. BOHEIMER. *British Medical Journal* [*Brit. med. J.*] **2**, 1514–1518, Dec. 25, 1954. 2 figs., 16 refs.

705. **Idiopathic Hypochromic Anaemia in Males**

J. W. B. FORSHAW. *British Medical Journal* [*Brit. med. J.*] **2**, 908–910, Oct. 16, 1954. 20 refs.

Idiopathic hypochromic anaemia in males is rare, only 11 cases being found among the records of two Liverpool hospitals for the period September, 1948, to January, 1954. These 11 patients, 9 of whom were seen personally by the author, were followed up for periods of between 4 months and 6 years, and the findings are discussed in the present paper. At the time of the first attendance at hospital 9 of the patients were under 25 years of age and 2 were aged 53 and 61. The blood picture in all the cases showed hypochromic anaemia with a colour index below 0·8; haemoglobin levels ranged from 8·5 to 4·4 g. per 100 ml., and in some cases the mean corpuscular haemoglobin concentration was very low. Possible causes of the anaemia are discussed. In every case the anaemia responded to administration of iron, in 9 of them to administration of iron by mouth only. No relapse was observed in patients followed up for more than 6 months.

These findings are in line with those of other workers—namely, that primary iron deficiency in males is a definite clinical syndrome. *M. C. G. Israëls*

706. **Intramuscular Iron Therapy in Iron-deficiency Anaemia**

I. M. BAIRD and D. A. PODMORE. *Lancet* [*Lancet*] **2**, 942–946, Nov. 6, 1954. 5 figs., 20 refs.

The effect of intramuscular administration of an iron preparation in patients with iron-deficiency anaemia was studied at the Royal Infirmary, Sheffield, with special reference to reactions, tolerance, absorption, and haematological response. A dextran–iron solution was used, 5 ml. of which was equivalent to 250 mg. of iron. All 10 volunteers on whom this was first tried experienced vague discomfort lasting 4 to 12 hours after the injection. There was staining of the skin in most of them, but this could be avoided by the use of a long needle and a Z-shaped track.

Of 40 patients with iron-deficiency anaemia, 38 responded adequately to intramuscular injections of this iron preparation. No reactions were observed in spite of serum iron levels as high as 13·8 mg. per 100 ml. The usual dose was 250 mg. once or twice daily to in-patients and twice weekly to out-patients to a total of 1,000 to 2,500 mg.

After a single intravenous injection the preparation disappeared from the serum more slowly than did saccharated iron oxide, and no difference was observed between anaemic patients and subjects without anaemia in the rate of fall in the serum iron level. In all cases the highest level was reached in 1 to 2 days, normal level being regained in 6 to 7 days. A mean calculation for the entire series showed that 100 mg. of iron was necessary to raise the haemoglobin level by 0·34 g. per 100 ml. The haemoglobin response to the injection varied considerably from patient to patient, a significant response being usually delayed for a week after the start of treatment. *E. G. Rees*

707. **The Relationship of Vitamin B_{12} and Folic Acid in Megaloblastic Anemias**

H. O. NIEWEG, J. G. FABER, J. A. DE VRIES, and W. F. S. KROESE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 118–132, July, 1954. Bibliography.

At the State University of Groningen the authors studied the serum level of cyanocobalamin (vitamin B_{12}) in 36 healthy subjects, 17 patients with pernicious anaemia in relapse, and 14 patients with other forms of macrocytic anaemia, *Lactobacillus leichmannii* being used for this purpose. Folic acid activity of whole blood was determined in 43 healthy subjects, at various times during treatment in 16 patients suffering from pernicious anaemia in relapse, and in the above-mentioned 14 patients with other forms of macrocytic anaemia, the technique employed being a modification of that of Teply and Elvehjem (*J. biol. Chem.*, 1945, **157**, 303).

In healthy subjects the serum values for total cyanocobalamin varied from 0·3 to 1·05 mμg. per ml.; in pernicious anaemia in relapse the values were 0·005 to 0·175 mμg. per ml. In other forms of megaloblastic anaemia reacting to treatment with cyanocobalamin the level was also low. In most cases which were refractory to administration of cyanocobalamin the vitamin level was normal.

The folic acid level of normal whole blood varied from 2·9 to 24·1 mμg. per ml., with an average of 8·05 mμg.; the level in 4 cases of sprue and one of megaloblastic anaemia of pregnancy was low. In these patients treatment with cyanocobalamin was ineffective, but all responded to administration of folic acid. In some patients reacting to administration of the vitamin (nutritional megaloblastic anaemia, megaloblastic anaemia of pregnancy, and gastro-colic fistula) the folic

acid level of the blood was normal. It was normal in half of the 16 cases of pernicious anaemia and low in the remainder. The effect on the blood folic acid level of intramuscular injection of cyanocobalamin was studied in 7 untreated cases of pernicious anaemia. The immediate effect was a fall in the folic acid level, in some cases within 2 hours of the injection; subsequently, after 72 hours or more, the level rose.

From the results the authors conclude that cyanocobalamin and folic acid interact as coenzymes at different stages of nucleic acid synthesis, and that the vitamin influences either the storage or the absorption of folic acid. *D. G. Adamson*

708. **Studies on Anemia of Disseminated Malignant Neoplastic Disease. I. The Hemolytic Factor**
G. A. HYMAN. *Blood* [*Blood*] **9**, 911–919, Sept., 1954. 2 figs., 13 refs.

An attempt was made to assess the part played by increased haemolysis in the production of anaemia in 34 patients suffering from widely disseminated neoplasia—Hodgkin's disease in 2, multiple myeloma in one, and carcinoma in the remainder. Anaemia of varying degree was present in 30, being moderate or severe in 17. Laboratory investigations, which included osmotic and mechanical fragility tests, the Coombs test, and estimation of the urinary and faecal urobilinogen excretion, reticulocyte count, and serum bilirubin concentration, revealed a significant degree of haemolysis in only 2 cases. There was a positive reaction to the Coombs test in only one case, in which, however, the other criteria for haemolysis were considered to be insignificant. The erythrocyte survival time was determined by the Ashby technique in 13 cases, and in 12 of them a considerable acceleration of erythrocyte destruction was observed.

It is concluded that the most sensitive method of detecting haemolysis is by the use of the Ashby technique, and that increased haemolysis is an important factor in the anaemia of neoplastic disease.

An incidental finding was the presence of tumour cells in 16 out of 23 adequate specimens of bone marrow obtained by aspiration. *L. J. Davis*

709. **ABO Heterospecific Pregnancy and Hemolytic Disease. A Study of Normal and Pathologic Variants. III. Hematologic Findings and Erythrocyte Survival in Normal Infants. IV. Pathologic Variants**
W. W. ZUELZER and E. KAPLAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 307–338, Sept., 1954. 7 figs., 22 refs.

From a study at the Wayne University College of Medicine, Detroit, details of 74 selected cases of haemolytic disease due to ABO incompatibility are tabulated and compared with those of 228 unselected infants born of heterospecific and homospecific pregnancies.

The authors conclude that ABO heterospecific pregnancy usually has no harmful effect on the foetus, but that the child may be affected when the maternal serum contains special immune antibodies. They also state that the presence in the serum of the newborn infant of free antibody antagonistic to its blood group is of diagnostic significance.

In about 15% of the selected cases kernicterus developed and was related to hyperbilirubinaemia. Four of the affected cases showed the so-called inspissated-bile syndrome. In all the cases of haemolytic disease the mother's blood was Group O and the infant's either Group A or B, and in each case where the infant's blood belonged to Group A_1 the maternal serum had Group-A_1 specificity. It is suggested that infants whose blood is of Group A_2 are not susceptible to haemolytic disease.

Secretion of the blood-group factors by the infants did not influence the picture. Erythrocyte survival studies demonstrated that in affected infants of Group A or B transfused Group-O cells were more slowly eliminated than cells of Group A or B, and this characteristic persisted for more than 30 days, although by this time free antibody was no longer demonstrable in the infant's serum. *John Murray*

LEUKAEMIA

710. **Acute Leukaemia Preceded by Myeloid Aplasia.** (Leucémies aiguës précédées d'une aplasie myéloïde)
B. DREYFUS and M. BESSIS. *Sang* [*Sang*] **25**, 787–797, 1954. 33 refs.

Some cases of acute leukaemia present as aplasia of the marrow, and in a review of 16 cases from the literature and one personal case the authors discuss the two possibilities (1) that such aplasia is itself a manifestation of acute leukaemia, or (2) that it is a definite disease which predisposes to the development of acute leukaemia. The former, classic, hypothesis is rejected, the authors assuming that the marrow aplasia is a symptom of arrest of maturation of the non-differentiated reticulum cells, whereas acute leukaemia indicates arrest of maturation at the haemocytoblastic stage. The second hypothesis receives more support from experimental observations, since it has been shown that the aplasia of the marrow in mice and guinea-pigs which follows a large single dose of *x*-irradiation can be cured, or alternatively can be prevented, by complete screening of the spleen or of the marrow of a single bone. *A. Piney*

711. **The Preleucoblastic Anaemia of Acute Leukaemia.** (Les anémies préleucoblastiques de la leucose aiguë)
J. BERNARD and M. BOIRON. *Sang* [*Sang*] **25**, 797–825, 1954. 3 figs., bibliography.

The authors present a well-documented review of the literature on the non-specific anaemia which sometimes precedes the development of leucoblastic acute leukaemia, emphasizing that they have included only cases in which neither the peripheral blood nor the bone marrow showed any signs of leukaemia. The anaemia is normochromic or slightly hyperchromic, with sometimes evidence of slight haemolysis, and it is often accompanied by moderate hypoplasia of the marrow. In a few cases auto-antibodies are present, but in some hypersplenism seems to be sufficient to explain the anaemia, while in others it is explained by severe leuco-

penia and/or thrombocytopenia. The authors describe three stages: (1) aplasia of the marrow, (2) a period of regeneration, and (3) the final leukaemic stage. They describe 7 of their own cases, with full haematological details. *A. Piney*

712. **The Aetiology of Acute Leukaemia. A Study of 193 Cases.** (A propos de l'étiologie de la leucose aiguë. Étude de 193 cas)
L. REVOL, C. MILLET, and —. THIVOLLET. *Sang* [*Sang*] **25**, 825–840, 1954. 6 figs.

The authors present the results of a study of the aetiological factors in 193 cases of acute leukaemia seen at various hospitals in Lyons during the 6-year period 1946–51. The patients' ages ranged from 2 to 80 years and 91 were female and 102 male. The factors chiefly considered were: (1) extrinsic factors, such as geographical distribution, annual incidence, family contacts, and predisposing conditions; (2) intrinsic factors, such as age, sex, and heredity of the patients. The authors conclude that the series was too small to permit of definite conclusions on many of the points, but there was evidence of a familial rather than hereditary character of the disease, and a noticeably increased incidence was observed in women at the menopause.

[Although no new facts were elicited, the paper is of value in amplifying our knowledge of some aetiological factors in leukaemia.] *A. Piney*

HAEMORRHAGIC DISEASES

713. **Acquired Antithromboplastinogenemia (Hemophilia-like Disease): with Special Reference to its Diagnosis**
A. J. QUICK, E. R. DANIELS, and C. V. HUSSEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 94–103, July, 1954. 1 fig., 21 refs.

The authors report the results of an investigation at the Marquette University School of Medicine, Milwaukee, of 2 cases of a haemorrhagic diathesis which was regarded as being due to a circulating anticoagulant distinct from heparin. It is pointed out that this condition can sometimes be distinguished from haemophilia by the addition of suspected plasma to normal blood, when the clotting time is prolonged; this is not observed when haemophilic plasma is added to normal blood. But reliance on this test alone in the 2 cases here described would have resulted in failure to establish the presence of the anticoagulant. The authors claim not only that detection can be made certain by the use of 2 other tests—the prothrombin consumption test and the thromboplastinogen titration test—but also that the concentration of the circulating anticoagulant can be estimated.

The prothrombin consumption time was determined on the serum after the clotting time had been estimated. The clotted blood was incubated for 15 minutes at 37° C., centrifuged at 2,000 r.p.m. for one minute, then returned to the water bath and the prothrombin time of the serum determined after 30 and 60 minutes. The thromboplastinogen titration test consists in adding increasing amounts of a standard preparation of thromboplastinogen to a series of test-tubes containing a fixed volume of blood, and in determining the prothrombin remaining in the serum after the blood is clotted under standard conditions. A small amount of thromboplastinogen will correct the defective prothrombin consumption in haemophilia, while a much greater quantity is required to increase the prothrombin consumption to normal in blood containing the anticoagulant. *D. G. Adamson*

714. **The Relative Incidence of Anti-hemophilic Globulin (AHG), Plasma Thromboplastin Component (PTC), and Plasma Thromboplastin Antecedent (PTA) Deficiency: a Study of Fifty-five Cases**
P. G. FRICK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 860–866, June, 1954. 2 figs., 14 refs.

Recent studies have shown that haemophilia, which had previously been regarded as a single disease entity, in fact includes three different entities: anti-haemophilic globulin (A.H.G.) deficiency, plasma thromboplastin component (P.T.C.) deficiency, and thromboplastin antecedent (P.T.A.) deficiency. In the light of these findings the author, at the University of Minnesota Hospitals, Minneapolis, has re-studied 55 cases, previously diagnosed as of haemophilia, with a view to determining the relative incidence of the three deficiencies. He found that in 45 of the 55 patients the clotting defect was due to A.H.G. deficiency, in 6 to deficiency of P.T.C., and in 4 to P.T.A. deficiency. He further found that A.H.G. and P.T.C. deficiencies are clinically indistinguishable, the range of severity of the haemorrhagic symptoms varying greatly in both. With regard to P.T.A. deficiency, he was able to confirm the finding of Rosenthal *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1953, **82**, 171; *Abstracts of World Medicine*, 1953, **14**, 223) that this is associated with a mild haemorrhagic diathesis occurring in both sexes. *John F. Wilkinson*

715. **Mild PTC (Plasma Thromboplastin Component) Deficiency Occurring in Two Brothers**
D. E. BERGSAGEL, S. S. SETNA, G. E. CARTWRIGHT, and M. M. WINTROBE. *Blood* [*Blood*] **9**, 866–874, Sept., 1954. 3 figs., 16 refs.

716. **Thrombohemolytic Thrombocytopenic Purpura**
E. ADELSON, E. J. HEITZMAN, and J. F. FENNESSEY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 42–60, July, 1954. 8 figs., 45 refs.

A description is given of a new case of "thrombohaemolytic thrombocytopenic purpura", a syndrome consisting of haemolytic anaemia, thrombocytopenic purpura, and multiple structureless thrombi in many small vessels throughout the body. Particular attention is directed to the presence among the erythrocytes of "helmet cells", which appear to be pathognomonic. No haemolysin or agglutinin could be demonstrated, but differential agglutination studies showed a greatly shortened erythrocyte survival time.

[This paper includes excellent photomicrographs and a full bibliography.] *A. Piney*

Respiratory System

717. **The Visco-elastic Properties of the Lungs in Acute Pneumonia**
R. MARSHALL and R. V. CHRISTIE. *Clinical Science* [*Clin. Sci.*] **13**, 403–408, Aug., 1954. 3 figs., 12 refs.

Simultaneous measurements of intra-oesophageal pressure, which closely follows intrapleural pressure, and of the rate of air flow at the mouth were made on 7 patients with acute pneumonia at St. Bartholomew's Hospital, London, on admission and repeatedly during the course of the illness and convalescence. The coefficient of elastic resistance (rigidity) of the lungs, which can be estimated from these measurements, was initially high and fell to normal during convalescence. It is argued that this rigidity of the lungs was partly due to changes in radiologically normal lung, the apparently consolidated areas not being voluminous enough to account for the greatly increased rigidity, and decreasing rigidity of the lungs during treatment not necessarily being correlated with clearing of the radiological shadows. Despite the increased rigidity of the lungs the respiratory swing in intrapleural pressure was little greater than normal because of the small tidal volume in acute pneumonia.

The mechanical work of breathing is normally minimal at a rate of about 15 breaths per minute. In acute pneumonia the rigidity of the lungs necessitates a higher respiratory rate and a small tidal volume if the mechanical work of breathing is to be as low as possible. Optimal respiratory rates were calculated in each case from the coefficients of elastic resistance and of viscous and turbulent airway resistance and ranged between 46 and 18 per minute; these figures agreed fairly well with the observed respiratory rates, which ranged between 52 and 13 per minute. *W. A. Briscoe*

718. **Respiratory Failure in Acute Chest Infections**
E. K. WESTLAKE. *British Medical Journal* [*Brit. med. J.*] **2**, 1012–1018, Oct. 30, 1954. 2 figs., 37 refs.

The investigation described in this paper was undertaken to determine the factors, other than infection, which influence prognosis in acute respiratory disease in bronchitic subjects.

In 30 patients with severe respiratory infection admitted to the Hammersmith Hospital, London, the oxygen content, carbon dioxide tension, and the *p*H of the arterial blood were estimated. In 5 out of 6 patients with lobar pneumonia but without a history of chronic respiratory disease the arterial CO_2 tension on admission was below normal (less than 35 mm. Hg); it was unchanged in one. In these cases there was generally a mild alkalaemia with slight arterial anoxaemia. This appeared to be the normal physiological response to respiratory infection.

In 14 bronchitic and emphysematous subjects without cardiac failure the arterial CO_2 tension on admission was below normal in only one patient and above normal (46·2 to 76·2 mm. Hg) in 9. There was moderate anoxaemia (oxygen saturation 50·8 to 90·6%), which persisted in 5 of the 10 survivors, and mild to moderate CO_2 retention with a *p*H within normal limits or slightly below. Both the *p*H and the arterial CO_2 tension returned to normal on recovery.

Cor pulmonale with congestive cardiac failure was present in 10 patients, all of whom had moderate to severe anoxaemia (oxygen saturation 38·4 to 81·4%), acidaemia (*p*H 7·22 to 7·38), and hypercapnia (pCO_2 51·7 to 86·5 mm. Hg). Mild anoxaemia persisted in the 4 survivors in this group, in 3 of whom there was also slight CO_2 retention.

Of 10 patients in whom on admission the arterial oxygen saturation was less than 70% and the CO_2 tension higher than 60 mm. Hg, only 3 recovered. The author considers that respiratory failure is present on admission when the initial arterial CO_2 tension is 5 to 32 mm. Hg higher than normal. The clinical picture in these cases of acute respiratory failure was distinctive: anoxaemia, hypercapnia, and acidaemia caused increased intracranial pressure, resulting in headache, papilloedema, mental confusion, restlessness, hallucinations, myoclonic twitching, and profuse sweating. Pulmonary hypertension increased cardiac output, and congestive cardiac failure also occurred.

Treatment consisted in adequate chemotherapy to counter the infection (especially infection due to *Haemophilus influenzae*); administration of oxygen to relieve anoxaemia; and relief of respiratory obstruction by antispasmodics, postural drainage, and coughing. The author points out the danger of carbon dioxide narcosis with oxygen therapy, and advises the use of a B.L.B. mask or lightweight "polymask" at 1 to 3 litres per minute. Mechanical ventilation proved ineffective for increasing the ventilation of patients in severe respiratory failure. *I. Ansell*

719. **Carcinoma (Cylindromatous Type) of Trachea and Bronchi and Bronchial Adenoma. A Comparative Study**
H. T. ENTERLINE and H. W. SCHOENBERG. *Cancer* [*Cancer* (*N.Y.*)] **7**, 663–670, July, 1954. 6 figs., 25 refs.

Two cases of the cylindromatous type of bronchial carcinoma are reported from the Hospital of the University of Pennsylvania, Philadelphia, and a comparison made of this tumour with the "carcinoid" type of bronchial adenoma by means of reference to well-documented cases in the literature. These two types of tumour are frequently classed together amongst the bronchial adenomata, but the authors believe that their differences in behaviour are so marked that a distinction between them should be made. The cylindromatous type of carcinoma usually occurs in a more proximal situation, such as the main bronchus or the trachea, its

infiltrative power is greater, it is more prone to local recurrence, and it may metastasize. It is suggested that the tumour probably arises from the ducts of mucous or salivary glands, and a similar form is therefore seen in the salivary glands, palate, and paranasal sinuses. Bronchial adenoma on the other hand arises more peripherally (never in the carina or trachea in this series) and is much less likely to recur locally or to give rise to metastases. *G. J. Cunningham*

720. **Pulmonary Adenomatosis**
S. M. FARBER, D. A. WOOD, F. SANGALLI, S. L. PHARR, and —. RUKMONO. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 483–491, Oct., 1954. 15 figs., 13 refs.

After discussing the nomenclature, aetiology, and clinical aspects of pulmonary adenomatosis, the authors describe in some detail the cytology of the sputum in this disease, with special reference to 4 cases seen in San Francisco hospitals since 1948. The aetiology of the condition is obscure, but the occurrence of local and distant metastases suggests that it is a carcinoma. This hypothesis, however, does not account for two characteristic features—namely, the preservation of the pulmonary structure, and the occasional long periods of apparent stabilization of the disease. Histologically, the lesion is composed of alveoli lined with columnar or cuboidal epithelial cells with eosinophilic cytoplasm and basally-placed nuclei. None of the symptoms, signs, radiological appearances, or laboratory findings is pathognomic.

The authors point out, however, that in as many as 80% of some large series of reported cases an abundance of diagnostic cells has been observed in the sputum. Large compact groups of cells arranged as acini may be seen, and these cells generally each contain one massive vacuole. Nuclear appearances are not suggestive of carcinoma. A case of pulmonary adenomatosis reported by Stephens and Shipman in 1949, in which the patient was known to have been in contact with sheep suffering from a condition known as *jaagsiekte*, is discussed on the basis of recent cytological examination of the patient's sputum. *E. G. Rees*

721. **The Respiratory Response to CO_2 in Emphysema**
F. J. PRIME and E. K. WESTLAKE. *Clinical Science* [*Clin. Sci.*] **13**, 321–332, Aug., 1954. 2 figs., 31 refs.

Partial pressures of oxygen and carbon dioxide were estimated in arterial blood samples taken at the Brompton Hospital, London, from 35 emphysematous patients after they had breathed successively air, oxygen, and 5% carbon dioxide in oxygen, each for long enough to reach a steady state of ventilation. In most cases the administration of oxygen led to a fall in minute ventilation and to a rise in arterial carbon dioxide tension (from an average value of 52 mm. to one of 60·6 mm. Hg).

On changing from oxygen to 5% carbon dioxide in oxygen, ventilation rose on the average from 8·9 litres per minute to only 21·8 litres per minute. This small response was apparently not due to the limit imposed by the maximum breathing capacity, which averaged 34·7 litres per minute. The more the carbon dioxide retention in the arterial blood, the less was the ventilatory response to inspired carbon dioxide. This insensitivity to inspired carbon dioxide is partly due to the high alkali reserve, which buffers changes in arterial *p*H, but it must also be partly due to insensitivity of the respiratory centre to changes in the *p*H and carbon dioxide tension of the arterial blood. *W. A. Briscoe*

722. **Early Tracheotomy in Secretional Anoxia**
R. W. TAYLOR. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 1–14, July, 1954. 38 refs.

In a preliminary discussion of the physiology of normal respiration the author points out that in addition to regulation of the medullary centres by the blood *p*H and arterial CO_2 concentration there is a secondary mechanism acting through chemoreceptors in the aortic and carotid areas, which are sensitive to lowered oxygen tension but are not depressed by accumulation of CO_2 or by opiates or barbiturates. Repeated anoxia has a cumulative effect, and even mild anoxia can cause permanent damage, particularly to cerebral tissues, if the arterial oxygen tension is not maintained. Loss of the cough reflex and of the swallowing reflex leads to accumulation of fluid, mucus, and saliva in the bronchial tree, which in turn prevents the normal exchange of oxygen between alveolar air and the blood, and thus produces anoxia.

From his experience at Vancouver General Hospital, the author has found that tracheotomy is the simplest method of relieving obstruction in such cases, its performance making tracheobronchial suction and direct supply of humidified oxygen much easier. For relief of anoxia, he states, " a prophylactic tracheotomy is preferable to a therapeutic one if clinical judgement indicates the necessity. The common denominator will be seen to be a respiratory depression with loss of the protective reflexes of the respiratory tract ". As indications for tracheotomy the author gives: (1) acute laryngotracheobronchitis or foreign bodies in the respiratory tract; (2) neurological disorders interfering with the respiratory reflexes, such as bulbar and bulbospinal poliomyelitis, paralysis in diphtheria, polyneuritis, or cerebral vascular accidents; (3) coma, with developing respiratory embarrassment, due to trauma or drugs; (4) injuries of the face or cervical spine, and crush injuries of the chest affecting the airway; (5) in the case of old and debilitated patients exposed to long operations prophylactic tracheotomy may lower mortality by preventing pulmonary and cerebral complications; and (6) conditions such as myasthenia gravis.

In cases of paralysis of the respiratory muscles a respirator is needed. The author suggests that the Emerson " demand-respirator " more closely imitates normal respiration than the Drinker type of respirator. Other methods of maintaining respiration are discussed and 10 of the author's cases are described. Particularly interesting among these are a case of fat embolism following multiple fractures and a case of basilar artery thrombosis. In both of these cases the patient recovered completely. *F. W. Watkyn-Thomas*

Otorhinolaryngology

723. **Congenital Laryngeal Stridor. A Diagnostic Study Including Technique of Tracheobronchography in Infants**
D. C. BAKER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 172–185, Aug., 1954. 6 figs., 39 refs.

Congenital stridor appears at, or shortly after, birth and may persist for one or two years. It has long been recognized that the noisy breathing troubles others more than it does the child, and has usually a benign and self-limiting course. It is usually agreed that the cause is a congenital malformation which, with the flaccidity of the parts in the infant, produces a valvular action of the back-folded epiglottis and the aryepiglottic folds.

A study of 83 cases of congenital laryngeal stridor seen at the Babies Hospital (Columbia University), New York, is presented; 58 were in males and 25 in females; in 69 the stridor was noticed at birth—only in 4 was the onset as late as the 6th week of life. In 76 cases the cause was an exaggerated infantile larynx with inspiratory laryngeal collapse, the other causes being abnormalities of the epiglottis or aryepiglottic folds, and (in one case) macroglossia.

It is most important to differentiate these forms of stridor from stridor due to constriction by some anomaly of the aorta or other vessel which may form a ring around the trachea, oesophagus, or a main bronchus. In such cases there is usually obstruction as well as stridor, especially during feeding. In anomalies of the heart the left main bronchus may be compressed, whereas a double aortic arch (" vascular ring ") causes compression of the trachea and oesophagus as the right and left arches pass to either side and unite behind to form the descending aorta. If the fourth right aortic arch persists, the aorta arches over the right main bronchus and runs down and to the right behind the oesophagus, instead of taking the normal course to the left and in front of it. Encirclement may be caused by an aberrant ligamentum arteriosus attached to a right arch or to persistence of the foetal left fourth arch. Anomalies of the left common carotid or of the left subclavian artery can compress the trachea or oesophagus. Of 6 infants with congenital anomalies of the aorta, 5 had stridor with attacks of cyanosis and dyspnoea during feeding, and 2 of these cases are reported in detail. In one a double aortic arch was found completely encircling the oesophagus and trachea; this was divided and the child made a good recovery. In the second case fibrous bands were seen in the region of the left innominate vein; the right innominate artery crossed the trachea diagonally from left to right and compressed it. There was heart failure at operation, and the child died a few days later.

A description is given of the technique of tracheobronchography in children, which the author considers to be safer and more satisfactory than bronchoscopy. He holds that an enlarged thymus should not be accepted as the cause of stridor on *x*-ray evidence alone; of the 83 cases he has studied, none was due to this cause.

F. W. Watkyn-Thomas

724. **Reevaluation of Air-conditioning from the Point of View of Otorhinolaryngology**
J. M. KINKADE. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 15–23, July, 1954. 39 refs.

The author comments on the increasing demand for air-conditioning and, noting that the engineering aspect is ahead of the medical valuation, points out that correct air-conditioning depends on control of humidity, air movement, and radiation, as well as of temperature. Poor control of indoor temperature may mean that there are different levels of temperature in a room; under such conditions patients liable to vasomotor rhinitis are liable to an attack. A marked difference between the controlled indoor temperature and the natural outdoor temperature, suddenly experienced, may cause " cold shock " or on the other hand " air-conditioning shock ". Humidity is discussed from the point of view of the patient with sinus disease or nasal allergy; there is considerable difference of opinion on the optimal humidity for such conditions. The author also offers some comments on " air sanitation ", but the practical difficulties seem considerable and the benefits doubtful. Ultraviolet radiation seems less effective than " washing " with a germicidal agent, and has the added disadvantage that it may cause the formation of ozone which, in excess, has an intoxicating effect. *F. W. Watkyn-Thomas*

725. **Benign Giant-cell Tumors of Skull and Nasal Sinuses**
R. PEIMER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 186–193, Aug., 1954. 7 figs., 14 refs.

The origin of giant-cell tumours of bone has been variously regarded as (1) traumatic, (2) inflammatory, and (3) neoplastic. Geschickter and Copeland suggest that they arise from hyperplasia of osteoclasts left at the site of an endochondral ossification, and that as the giant cells represent osteoclasts the tumour is best described as an osteoclastoma. Jaffe, Lichtenstein, and Portis, on the other hand, regard them as neoplasms arising from undifferentiated supporting tissue of the marrow. Such tumours are not uncommon in the long bones, small bones, and vertebrae of young adults, but involvement of the sinuses or bones of the cranial vault, of which 3 cases are reported in this paper, is seldom found.

In the first case a mass in the antral wall above the roots of the 1st and 2nd molars, firmly attached to all walls except the medial, was removed; there was no

recurrence after 8 months. In the second there was a mass in the ethmoid eroding the sphenoid bone, causing nasal obstruction, proptosis, and diplopia, with a history of injury a few months before any symptoms were noted; treatment with deep *x*-ray therapy left the symptoms unchanged. In the third case a tumour arising in the roof of the orbit, causing proptosis but no other symptom, was removed, but apparently not completely; a course of deep *x*-ray therapy was therefore given and there has been no recurrence after 20 months, but the eye is still proptosed. *F. W. Watkyn-Thomas*

726. **Olfactory Esthesioneuroepitheliomas of Louis Berger**
L. FRÜHLING and C. WILD. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 37–48, July, 1954. 10 figs., 18 refs.

Neurogenic nasal tumours may arise from the sympathetic fibres, from the nerve axons, or from the sphenopalatine ganglion. In 1924 Berger described a tumour resembling the "neuraxo-epithelioma" of Masson, characterized by the presence of true cavities (the "neuroepithelial rosettes"), which had its origin in the olfactory organ. In most of the cases of nerve tumours of the nose hitherto reported there were other possible sites of origin. The present authors believe that in the true neurogenic tumour of the nasal fossae originating in the olfactory organ neuroepithelial rosettes are present, and they describe 4 such cases seen at the Institute of Pathological Anatomy, Strasbourg.

In all 4 cases there was a firm, polypoid mass obstructing one nasal fossa, usually painless, with little bleeding and complete anosmia on the affected side. In one case, where the mass was ulcerated, there was free haemorrhage, and in another there was a stalk from the olfactory region. One case was not followed up, but experience in the others indicated that the growth was highly radiosensitive and did not appear to metastasize. The treatment of choice is surgical ablation followed by a course of heavy *x*-irradiation. The results were good.
F. W. Watkyn-Thomas

727. **Epistaxis Controlled by Combined Ligation of the External Carotid and Anterior Ethmoidal Arteries. Report of a Case of Severe Epistaxis Occurring Seven Days following Head Injury**
S. PELUSE and H. W. FISHLER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 74–79, July, 1954. 1 fig., 6 refs.

The authors describe, from Los Angeles County Hospital, the case of a patient who accidentally struck his left occipital area against a metal chute. He experienced a momentary "black-out" and a sudden pain in the vertex but went on working. The pain persisted for a week, and at the end of this period he bled from the left nostril; later, the pain became unbearable, and that night he bled so severely that he was admitted to hospital. Bleeding from the nose and mouth continued in spite of transfusions and packing. On the 14th day both branches of the external carotid artery on the left were tied. (The superior thyroid artery was absent.) When the packing was removed the bleeding became more profuse than before and the anterior ethmoidal artery was therefore exposed and tied, whereupon bleeding stopped immediately.

The authors remark that this case confirms the earlier observation of Macbeth (*J. Laryng.*, 1948, **62**, 42) that in head injury there is often bleeding from the anterior ethmoidal artery or its branches, since these lie in bony canals and cannot contract; further, that injury may not cause haemorrhage until the damaged vessel has been eroded by infection. An interesting point is the apparent triviality of the causal injury. The authors suggest that damage to the ethmoidal region was by contrecoup. [In the abstracter's opinion it is more likely that a fissured basal fracture spread forward to the ethmoid.]
F. W. Watkyn-Thomas

728. **Effect of Antibiotic Therapy on Mucoviscidosis. A Bacteriologic Study**
M. R. H. STOPPELMAN and H. SCHWACHMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 759–763, Nov. 4, 1954. 46 refs.

729. **Ménière's Disease Treated by Portmann's Operation. Report and Clinico-pathological Study of a Case**
C. S. HALLPIKE and M. S. HARRISON. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 141–144, Aug., 1954. 6 figs.

The case is described of a woman of 50 on whom Portmann's operation was performed for Ménière's disease at the County Hospital, Lincoln. The saccus endolymphaticus was successfully opened—it was divided where it passed from bone to dura, as was proved post mortem—but the patient remained in coma after operation and died 3 days later. Examination of the cochlea showed two points of interest. (1) Although it is now usually believed that the deafness in Ménière's disease is caused by changes in the organ of Corti, it has not hitherto been possible to show definite changes in the hair cells. In this case Corti's organ was found to be shrunken, with disorganization of the outer hair-cell complex. (2) Although the endolymph had escaped from the divided saccus, Reissner's membrane had not returned to the normal position.

The latter finding does not necessarily invalidate the theoretical basis of the operation, since prolonged stretching of the membrane might lead to its growth so as to allow it to occupy the new position without tension. "In other words, the bulging of Reissner's membrane . . . cannot be taken to mean a raised endolymph pressure at the time of the patient's death. It means only that in the past there was a raised pressure forcing the membrane into its new position. Thus Portmann's operation, carried out in a case of established Ménière's disease, would not of necessity cause any change in the position of Reissner's membrane. Nevertheless, should any further outpouring of endolymph occur, then, instead of causing a further displacement of Reissner's membrane, it would be discharged through the open saccus with minimal pressure changes in the labyrinth, and so, the purpose of Portmann's operation would be fulfilled". *F. W. Watkyn-Thomas*

Urogenital System

730. **Reabsorption from Urine in Colon. Experimental Studies on Some Patho-physiological Conditions following Ureterocolic Anastomoses**

M. PERS. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] 6, 189–202, 1954. 9 figs., 23 refs.

Experiments were carried out at the Finsen Institute and the University of Copenhagen with the aim of studying the reabsorption from the colon of various components of urine under the conditions which might arise after transplantation of the ureters. Into an isolated portion of large intestine in the abdomen of a dog 50-ml. samples of urine were introduced and left *in situ* for 2 hours. It was found that when the specific gravity of the urine was more than 1·019 the volume of fluid increased, whereas it decreased or remained unchanged if the specific gravity was lower. When the urinary chloride concentration was less than that in the plasma 75 to 100% of the chloride was absorbed from the urine, the proportion absorbed being lower at higher levels of urinary chloride content. The net absorption of chloride exceeded that of sodium. The absolute quantity of urea reabsorbed was almost constant and appeared to be independent of the concentration of urea in the urine.

It is suggested that the hyperchloraemic acidosis which occurs in patients with transplanted ureters when renal function is impaired may be attributable in part to production of urine of low concentration, which favours the reabsorption of a high proportion of its content of chloride. *G. Loewi*

731. **Osteosclerosis Associated with Chronic Renal Failure**

T. CRAWFORD, C. E. DENT, P. LUCAS, N. H. MARTIN, and J. R. NASSIM. *Lancet* [*Lancet*] 2, 981–988, Nov. 13, 1954. 11 figs., 15 refs.

Although rickets, osteomalacia, and osteitis fibrosa are the commonest bone changes in chronic renal disease, osteosclerosis has also been noted to occur. In the present paper 3 further cases of osteosclerosis associated with chronic renal disease are described. The first patient, a man of 42 who died in uraemic coma due to chronic pyelonephritis, had had nocturia for many months before being admitted to hospital with a complaint of backache. Chemical analysis of the blood revealed a reduced calcium level, normal inorganic-phosphorus level, and high alkaline-phosphatase level. Radiologically there was a generalized increase in the density of the skeleton. Bone biopsy (iliac crest) showed hyperostosis with little fatty marrow. At necropsy no parathyroid glands were found. The second patient, a 17-year-old girl, died in uraemia due to chronic nephritis. Radiographs taken during the last month of life showed recent increased density of the spine and long bones. The plasma urea and inorganic-phosphorus levels were raised, the alkaline-phosphatase content was normal, and the calcium level was low. At necropsy only one small parathyroid gland was found. Sections of bone taken from ribs and vertebral bodies showed an abnormally dense structure; bone lamellae were broad and heavily calcified; osteoblasts were present in large numbers but osteoclasts were scanty. The third patient, a 26-year-old man, died in uraemic coma due to bilateral hydronephrosis. He had a congenital deformity of the spine and spinal cord which had resulted in bladder paralysis. Radiographs showed sclerosis of the vertebral bodies but osteitis fibrosa elsewhere in the skeleton. The blood levels of urea, alkaline phosphatase, and inorganic phosphorus were raised, while the calcium level was low. At necropsy 3 parathyroid glands were found, all of which were grossly enlarged. It was noted that the second and third patients had hypogonadism and disproportionately long limbs.

The authors are unable to explain the association of chronic renal failure and osteosclerosis. They suggest that, since the bones particularly affected were those mainly containing haematopoietic marrow, long-standing anaemia due to nitrogen retention may somehow have been related to the osteosclerosis. *K. G. Lowe*

732. **Disturbances of the Plasma Proteins in Kidney Disease.** (Perturbations des protéines plasmatiques au cours des néphropathies)

M. F. JAYLE, G. LAGRUE, and G. BOUSSIER. *Presse médicale* [*Presse méd.*] 62, 1246–1248, Sept. 22, 1954. 10 figs., 5 refs.

The authors have investigated the character of the plasma proteins in 23 samples of blood collected from 12 children in the oedematous stage of lipoid nephrosis, 8 samples from 7 children in a clinical remission of lipoid nephrosis, 7 samples from 4 adults in the oedematous stage of lipoid nephrosis, 9 samples from 8 children with acute glomerulonephritis, 20 samples from 20 patients with chronic nephritis, and 14 samples from 11 patients with nephrosis associated with renal insufficiency. Each blood sample was examined by paper electrophoresis and its so-called "protein table" obtained. The "protein table" was prepared from a knowledge of the total protein, albumin, and fibrinogen content of the sample and the results of determination of haptoglobin content, Verne's resorcinol index, and Kunkel's phenol index, and of McLagan's thymol test and two γ-globulin opacity tests.

For every nephrotic condition, there was an increase in the haptoglobulin value and the non-haptoglobulin fraction of α_2 globulin. The diagnostic value of Kunkel's lipoprotein test is discussed. The results for the chronic nephritis cases were more variable than those for the other groups. *J. E. Page*

Endocrinology

733. **Study of the Extrathyroidal Effects of Thyroid-stimulating Hormone**
L. H. KYLE, W. C. WELHAM, P. D. DOOLAN, and M. SCHAAF. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 1029–1038, Sept., 1954. 4 figs., 30 refs.

It has been shown that the pituitary thyroid-stimulating hormone (T.S.H.) exerts certain effects upon metabolism which are not mediated through the thyroid gland. The present authors report an investigation of the metabolic effect of administration of T.S.H. in 2 cases of myxoedema. Alterations in the proportions of fat, water, and solids in the body were estimated by the body specific gravity technique, which has already been described by the authors (*Clin. Res. Proc.*, 1953, **1**, 44). Water, electrolyte, and nitrogen balances were determined during the study, and the blood concentrations of ketones, pyruvic acid, amino-acids, and lipids were estimated daily. No changes in metabolism were observed in either of the 2 cases during administration of T.S.H.; definite changes were, however, noted after administration of thyroid extract. It is concluded that T.S.H. exerts a significant metabolic effect only when functioning thyroid tissue is present. *Nigel Compston*

734. **Calorigenic Effects of Single Intravenous Doses of L-Triiodothyronine and L-Thyroxine in Myxedematous Persons**
C. M. BLACKBURN, W. M. MCCONAHEY, F. R. KEATING, and A. ALBERT. *Journal of Clinical Investigation* [*J. clin. Invest.*] 33, 819–824, June, 1954. 4 figs., 15 refs.

A comparison was made of the calorigenic effects of single intravenous doses of L-triiodothyronine and L-thyroxine in 8 cases of untreated myxoedema. Triiodothyronine in doses above 4 μg. per kg. body weight produced malaise, restlessness, generalized aching, loss of appetite, and headache, the effects being similar to those seen in myxoedematous patients whose metabolic rate has been rapidly elevated by administration of desiccated thyroid. After the injection of triiodothyronine the metabolic rate rose more rapidly and to a higher level than after an equimolar dose of thyroxine, the maximnm level being reached within 48 to 72 hours (mean $2{\cdot}2 \pm 0{\cdot}1$ days), whereas with thyroxine it was reached only after 6 to 13 (mean $9{\cdot}4 \pm 0{\cdot}9$) days.

Measured in terms of the maximum metabolic level reached, triiodothyronine proved to be 3 or 4 times as potent as thyroxine.

The metabolic rate decreased after reaching the maximum level, and the dissipation of calorigenic effect was much more rapid after triiodothyronine than after thyroxine, the half-value times for triiodothyronine ranging from 4·0 to 9·7 days (mean $7{\cdot}4 \pm 0{\cdot}6$), but for thyroxine from 9·0 to 12·4 (mean $11{\cdot}9 \pm 0{\cdot}4$) days. Thus the metabolic effect of thyroxine long outlasted that of triiodothyronine, but measurement of the total amount of increased energy production in calories throughout the time of action of the compounds showed that the total caloric response after injection of small doses of triiodothyronine exceeded that produced by an equimolar dose of thyroxine. When large doses were given, however, the reverse occurred and thyroxine produced a greater total caloric response.

Richard de Alarcón

735. **The Role of the Thyroid Gland in the Regulation of Haematopoiesis.** (La posizione della tiroide nella regolazione dell'emopoiesi)
P. LARIZZA and G. CHIRICO. *Haematologica* [*Haematologica*] **38**, 771–846, 1954.

ADRENAL GLANDS

736. **The Use of Corticotrophin Gel as a Test of Adrenal Cortical Function**
J. D. N. NABARRO. *Lancet* [*Lancet*] **2**, 1101–1104, Nov. 27, 1954. 7 figs., 12 refs.

In carrying out tests for the diagnosis of Addison's disease the response of the adrenal cortex to stimulation with adrenocorticotrophic hormone (ACTH) has been shown to be influenced by the method of administration of the hormone. The author, who points out that intravenous infusion of the preparations of ACTH at present available is not without danger, has employed a recently introduced long-acting ACTH gel preparation injected intramuscularly; he found that the best effects were obtained with a dosage of 120 units given on successive days. The adrenal response was estimated by determining the number of circulating eosinophil leucocytes, the ratio of urinary sodium to potassium excretion, and the level of 17-ketosteroid excretion, the following changes being regarded as significant: (1) a fall in the absolute eosinophil count from over 50 per c.mm. to 10 or fewer per c.mm.; (2) a reduction of the urinary sodium:potassium excretion ratio to 50% or less of the initial level; and (3) an increase in urinary 17-ketosteroid excretion of 4 mg. or more per 24 hours.

In a study carried out at University College Hospital, London, on 33 patients whose adrenocortical function was presumed to be normal, all of them showed significant alterations in the absolute eosinophil count or in the urinary sodium:potassium excretion ratio, or both, after the first or second injection of ACTH gel. The excretion of 17-ketosteroids was increased significantly in all but 4 cases after the second injection, and probably would have been increased in all after a third injection. On the other hand, 4 patients with Addison's disease and 2 who had undergone total adrenalectomy showed no response after 3 to 6 injections of ACTH gel, while

6 patients with panhypopituitarism responded after intervals of from one to 6 days. Finally, 3 patients suffering from adrenocortical atrophy as a result of prolonged treatment with cortisone showed a normal response to the test.

It is concluded that the absence of any significant change in the three indices mentioned above after three consecutive daily injections of 120 units of the ACTH gel strongly supports a diagnosis of Addison's disease. A suggested procedure for carrying out the test is briefly outlined. *A. C. Crooke*

737. **Convulsive Seizures Complicating Cortisone and ACTH Therapy: Clinical and Electroencephalographic Observations**

H. L. WAYNE. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 1039–1045, Sept., 1954. 3 figs., 12 refs.

The literature contains a number of references to the occurrence of convulsive disorders during administration of ACTH (corticotrophin) and cortisone. There is no agreement, however, concerning the effect of these drugs upon the electrical activity of the brain, some workers having found that abnormalities are enhanced and others that they are suppressed.

At the Veterans Administration Hospital, Bronx, New York, the author studied the pattern of the electroencephalogram (EEG) in 43 non-epileptic patients before, during, and after treatment with ACTH and cortisone. When the EEG was normal before treatment only minor changes were observed in response to the drugs. In patients with an initially abnormal EEG gross changes tended to appear during treatment. In 4 of the latter cases, which are reported in detail, convulsions occurred. The author discusses the mechanisms involved in the production of the convulsions. *Nigel Compston*

738. **Adrenalectomy for Hormone Dependent Cancers: Breast and Prostate**

S. CADE. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **15**, 71–107, Aug., 1954. 19 figs., 38 refs.

After reviewing the literature on the effect of sex hormones on cancerous growths the author reports 50 cases of "hormone-dependent" cancer treated by adrenalectomy at the Westminster Hospital, London. Of these, 46 were of breast cancer, 2 of carcinoma of the prostate, and 2 of malignant melanoma; there were also 5 cases of malignant hypertension.

The technique of the operation is described. The author considers that the best exposure is obtained by a postero-lateral approach, the incision being made over the 12th rib, which, after division of the muscles, is excised. The total number of operative deaths was 9, all but one in cases of breast cancer—a mortality of 16%. From the fact that a much greater proportion of the deaths occurred after the bilateral operation in one stage than after a two-stage operation the author concludes that the latter is the safer procedure.

All the 46 patients with cancer of the breast were in the more advanced stages of the disease, some in the terminal stages. Of the 38 patients who survived the operation a successful result is recorded in about 50%, of whom half showed a very remarkable improvement. Subjective evidence of improvement was obtained from two-thirds of the patients, the most striking features being relief of skeletal pain and a sense of well-being. Some patients who were bed-ridden returned to a near-normal life. Objective improvement was assessed by regression or disappearance of obvious and easily detectable lesions, such as cutaneous or subcutaneous tumours, intra-abdominal masses, or intra-ocular metastasis.

"The assessment of results from adrenalectomy showed that patients fall into three groups: (1) those with remarkable, dramatic, and in many ways surprising improvement; in this series of 38 patients [who survived operation] 9 fall in this category, or 23·7%; (2) those in whom the improvement, although satisfactory, is less dramatic and incomplete, in whom new lesions appear whilst the existing ones fade away, where relief of pain is not quite complete with occasional exacerbations; there were 12 patients in this group, or 31·6%; (3) a group of patients in whom no improvement followed the operation, where no subjective or objective benefit was noted. These primary and total failures account for 11 patients, or 28·9%. These patients survived 1 to 5 months . . ."; 6 recent cases were not assessed.

No method was found of determining preoperatively which patients were likely to benefit from adrenalectomy. *A. G. Riddell*

DIABETES MELLITUS

739. **Fetal Mortality in Diabetic Pregnancies**

J. PEDERSEN. *Diabetes* [*Diabetes*] **3**, 199–204, May–June, 1954. 12 refs.

The author reports, from the Rigshospital, Copenhagen, a study of 161 diabetic mothers who gave birth to 192 infants in 189 deliveries. These patients were divided into two groups according to the stage of pregnancy at which they first attended the diabetic clinic, all those seen earlier than a minimum of 53 days from the calculated date of confinement being classed as having "long-term" treatment and those not seen until later as having "short-term" treatment. All patients were examined for retinopathy and cataract, and examined radiologically for evidence of peripheral arterial calcification. Treatment aimed at keeping the blood sugar as near the physiological level as possible, preventing acidosis and hypoglycaemia, and combating toxaemia and oedema. The diet supplied about 2,000 Cal. and contained 175 to 200 g. of carbohydrate, 80 to 90 g. of protein, and 80 g. of fat. Adequate doses of insulin were given, the average daily requirement being about 70 units. No hormones, mercurial preparations, ammonium chloride, or rutin were employed in treatment.

Until the 5th month of pregnancy the patients were seen at 3-weekly intervals, and thereafter weekly until 8 weeks before the calculated term, when they were admitted to hospital for observation. Delivery was usually induced about 3 weeks before full term either by drugs or by rupture of the membranes. Forceps

deliveries were common, but Caesarean section was performed in only 8% of the cases; at birth all the babies were at once placed in incubators, given oxygen, and fasted for 24 hours.

Among the mothers the incidence of severe diabetes was 63%, diabetic retinitis 23%, and calcified arteries 5%; the incidence of toxaemia was 30% and of hydramnios 50%. Nearly half (44%) of the mothers were primiparae. The total foetal mortality rate in the series was 26%. Mortality was shown to be correlated with duration of the diabetes as follows: 0 to 9 years' duration, 23%; 10 to 19 years, 30%; 20 years or over, 45%; it was also high in the presence of diabetic retinopathy (42%). It was notable, however, that there was a marked difference in the foetal mortality between the long- and short-term treated groups. In the long-term cases, it was 11% and 9% respectively for birth weights of 1 and 2·5 kg., whereas in the short-term cases the comparable figures were 36% and 25% respectively. The author claims that without sex-hormone therapy and without any extensive use of Caesarean section it is possible to obtain results as good as those reported by other workers. He considers that only in cases in which there are severe vascular changes should the mortality among infants of long-term treated mothers exceed 10%.

J. Lister

740. **Diurnal Rhythm in Severe Diabetes Mellitus. The Significance of Harmoniously Timed Insulin Treatment**
J. MÖLLERSTRÖM. *Diabetes* [*Diabetes*] 3, 188–191, May–June, 1954. 5 figs., 8 refs.

Drawing on his experience at the Swedish Diabetic Clinic, Stockholm, the author describes how in 1928 he observed diurnal variations of the blood and urine sugar levels in a diabetic patient. After determining that a diurnal rhythm of carbohydrate metabolism is a normal physiological phenomenon, he evolved a method of "harmoniously timed" insulin treatment based on the diurnal variations of urinary sugar excretion level. He also found variations in the excretion of ketone bodies and formation of ammonia in different patients and noted a recurrent peak in β-hydroxybutyric acid excretion. On the basis of these observations he has divided his diabetic patients into three types: (A) diabetes characterized by ketone excretion and sufficient ammonia formation; in these cases there is no danger of coma; (O) diabetes with ketone excretion but poor formation of ammonia; this is a grave type of the disease and coma will ensue if insulin is withheld; (B) diabetes without ketone excretion; this generally indicates a mild form of the disease.

From a statistical analysis of 2,116 cases it was shown that Type O is frequent in childhood and less common in old age, Type B is most common in the aged and uncommon in childhood, while Type A shows no characteristic age distribution. The author considers that it is important to recognize the diurnal rhythm of carbohydrate metabolism when treating diabetics, but stresses that it is also essential to know whether or not ketone bodies are formed in a given case and whether the amount of ammonia being formed is sufficient protection against acidosis and coma. To illustrate this point he quotes the case of a diabetic patient who suffered hypoglycaemic reactions, but when the insulin was decreased there was a tendency to acidosis. On studying the ketone formation in this case a periodic excretion of β-hydroxybutyric acid was found to occur. When insulin administration was adapted to the rhythm of excretion of β-hydroxybutyric acid, the diabetes came under perfect control.

J. Lister

741. **The Use of Insulin Aerosols in the Treatment of Diabetes.** (Über die Verwendung von Insulin-Aerosolen bei der Behandlung des Diabetes)
C. FAELLI. *Zeitschrift für Aerosol-Forschung und -Therapie* [*Z. Aerosol-Forsch.*] 3, 309–317, Aug., 1954. 21 figs.

It is suggested that the administration of insulin in aerosol form may offer great advantages, at least theoretically, and especially in children. Such an insulin aerosol was tested on 21 children with diabetes of moderate severity at the National Children's Diabetic Clinic, Rome, the effect of doses of 10 to 30 units given by injection being compared with that of the same doses administered as aerosol. A good response to the latter was shown in 16 (80%) of the cases.

Blood sugar curves after 20 g. of glucose by mouth and 0, 10, 20, and 30 units of insulin respectively by each method in 20 cases are given. The results with aerosol administration were very variable, being as good as with subcutaneous administration in some cases while in others they were inconstant, suggesting that the dose was not consistently absorbed. There was no response to the aerosol in 4 cases, some benefit in 10, and results comparable to those obtained with subcutaneous insulin in 7.

C. L. Cope

742. **Persistence of Normal Blood Sugar Level in a Number of Diabetics after Adequate Treatment with Insulin and a Free Diet.** (Persistance d'un parfait équilibre glycémique chez plusieurs diabétiques soumis à une insulinothérapie suffisante avec alimentation libre)
—. GILBERT-DREYFUS, J. C. SAVOIE, H. CHIMENÈS, and J. SEBAOUN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] 70, 707–717, June 18, 1954.

For long, following the work of Minkowski, the diabetic state has been considered to be the result of a diminished capacity of the cell to utilize glucose. In recent years, however, Soskin and others have suggested a quite different conception, namely, that the fundamental cause lies in some change which makes it difficult for glucose to pass through the cell membrane.

The present authors, who support Soskin's theory, report 7 cases in which they first stabilized the diabetes on what they term a "mixed regimen", consisting in a diet containing 150 to 200 g. of carbohydrate, the dose of insulin being increased until stabilization was achieved. They then replaced this regimen by a " glucose regimen " in which the patient received a daily carbohydrate intake of more than 400 g., but no insulin. In 6 of the 7 cases there was no deterioration in the blood sugar level on changing from the mixed regimen to the glucose regimen;

these 6 patients were finally instructed to eat what they wished and to take the insulin dose on which they were originally stabilized.

It is stressed that these were all cases of severe diabetes, the daily insulin requirements ranging from 30 units to 108 units. Furthermore, the criteria for stabilization were rigid, no blood sugar level above 200 mg. per 100 ml. being regarded as satisfactory. In their discussion the authors offer no explanation for these remarkable results. They add that although they have no intention of abandoning the accepted methods of treatment for the majority of cases of diabetes they consider that the method described is full of practical possibilities and may help in elucidating the pathogenesis of the diabetic state. *J. Lister*

743. **The Design of Insulin Trials. A Polylysine Insulin**
G. R. FRYERS, R. G. PALEY, and R. E. TUNBRIDGE. *Lancet* [*Lancet*] **2**, 782–784, Oct. 16, 1954. 2 figs., 7 refs.

In this report from the University of Leeds the authors describe their attempts to devise a satisfactory method for testing new types of insulin. It is pointed out that the wide variations in insulin-sensitivity of individual diabetics makes precise comparison of different insulins impossible; this is particularly so if the assessment is made on a random selection of diabetic subjects, including both the stable and the unstable, by comparison of mean blood sugar levels. It is also clear that any assessment based on observations made during a single day will leave out of account the variability of the blood sugar level from one day to the next.

In testing a new type of insulin, insulin X, the authors carried out two separate trials. For the first a small group of patients who were well controlled on a single dose of protamine zinc insulin (P.Z.I.) was chosen. On a series of three even dates each patient was given one of the insulins under test (P.Z.I. and two varieties of insulin X), and on the intervening odd dates their normal dose of P.Z.I. The blood sugar level was determined at 5 fixed times during each even day, and the mean deviation from the daily mean blood sugar level plotted. It was shown that the action of insulin X one-isophane was more rapid than that of insulin X two-isophane and P.Z.I., and that although the difference between P.Z.I. and insulin X two-isophane was slight, the former was somewhat slower in action. For the second study a group of unstable diabetics was selected. After satisfactory control with a mixture of equal parts of soluble insulin and P.Z.I. had been confirmed, blood sugar estimations were carried out at 4 fixed times on 4 consecutive days. A mixture of equal parts of soluble insulin and insulin X two-isophane was then substituted, and after an adjustment period of 3 days the process was repeated for another 4 days. Comparison of the mean deviations from the mean daily blood sugar level showed that the second mixture gave better control in the middle of the day, but less good control in the evening, than the first.

It is suggested that this method, which takes account of all variations in blood sugar level, should be used for the preliminary assessment of all new insulins to eliminate confusion, and that unstable diabetics should be chosen for such studies. *J. N. Harris-Jones*

744. **The Design of Insulin Trials. Insulin–Zinc Suspension (Lente)**
R. G. PALEY. *Lancet* [*Lancet*] **2**, 784–787, Oct. 16, 1954. 5 figs., 11 refs.

Assessment of insulin–zinc suspension (I.Z.S.) by the method previously described [see Abstract 743] failed to show that it gave smoother control than a mixture of protamine zinc insulins. It is concluded that whereas I.Z.S. may modify the blood sugar curve, it cannot control the essential stability of the diabetes in certain cases.

In the course of the investigation a striking change in the diabetic pattern of two patients was demonstrated, the variability of their blood sugar levels at different times after insulin undergoing a significant change over a period of some months. It is emphasized that in a comparative study of different types of insulin, care should be taken to avoid delay between the trials in order to eliminate the risk of a spontaneous change in the diabetic pattern. *J. N. Harris-Jones*

745. **Mauriac's Syndrome.** (A propos du syndrome de Mauriac)
M. BERNHEIM, R. FRANÇOIS, and J. LAMY. *Presse médicale* [*Presse méd.*] **62**, 1423–1424, Oct. 23, 1954.

In 1930 Mauriac [no reference given] described a syndrome consisting of hepatomegaly, obesity, and infantilism occurring in diabetic children; the present communication is a dissertation on Mauriac's syndrome. The condition usually occurs in children with severe and unstabilized diabetes mellitus. Hepatomegaly is the main feature found on examination, and inquiry may reveal a history of abrupt cessation of growth in a previously normally developing child; obesity may develop later. The different aetiological theories are discussed and the authors tentatively suggest that the syndrome may be due to (1) insufficient carbohydrate in the diet, (2) excess fat in the diet, and (3) inadequate insulin control.

They describe 6 cases in all of which the hepatomegaly, infantilism, and obesity disappeared after a " free diet " had been instituted and the daily dose of insulin regulated. Liver biopsy in one case showed fatty infiltration and in another early portal cirrhosis. The authors cast considerable doubt on the actual existence of Mauriac's syndrome, and infer that these symptoms and signs can occur singly or in combination in many diabetic children. They consider that the results in the cases described favour a " free diet " [but the better control of the diabetic state alone might explain the disappearance of the features of Mauriac's syndrome]. *I. McLean Baird*

746. **Diabetic Cataract and Cataract in the Diabetic.** (Cataracte diabétique et cataracte chez le diabétique)
J. SÉDAN and G. FARNARIER. *Diabète* [*Diabète*] **2**, 192–194, Nov.–Dec., 1954.

The Rheumatic Diseases

747. Three Cases of Collagen Disease Treated with Corticoids

D. G. RICHARDS. *British Medical Journal* [*Brit. med. J.*] 2, 777–780, Oct. 2, 1954. 8 refs.

The author describes 3 cases of diffuse collagen disease seen at the Queen Elizabeth Hospital, Birmingham, 2 of which were ultimately thought to be cases of acute disseminated lupus erythematosus and one to be a case of systemic scleroderma. He emphasizes the difficulty of diagnosis when the onset of the illness is extremely acute and the general constitutional disturbance is so severe that it masks the focal manifestations which are a guide to diagnosis in less acute cases. In all 3 cases the response to administration of corticoids was marked. The author believes that the hormones were probably life-saving, and suggests that the response to cortisone is of some diagnostic significance in these cases. *Nigel Compston*

748. Epidemiological Relationships between Scarlet Fever and Acute Rheumatism. (Über epidemiologische Beziehungen des Scharlachs zum akuten Rheumatismus) E. HÄSSLER. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] 13, 215–221, Aug., 1954. 1 fig., 15 refs.

The association between scarlet fever and acute rheumatism formed the subject of a study carried out in the German town of Chemnitz between 1950 and 1953. During that period an increase in the incidence of scarlet fever was accompanied by a parallel increase in that of acute rheumatism. Whereas 10 cases of acute rheumatism were reported in each of the years 1946 and 1947 (when there was no scarlatina epidemic), the figure for 1950 was 117 and for 1951 100. Although few of the patients developing rheumatic fever showed any signs of a prodromal scarlatiniform eruption, 22 children with scarlet fever (usually slight) showed evidence of cardiac damage without joint involvement, and in a few others chorea minor was noted. A plea is made for early and intensive penicillin therapy in all haemolytic streptococcal infections. *D. Preiskel*

749. The C-Reactive Protein Determination as a Measure of Rheumatic Activity

N. H. SHACKMAN, E. T. HEFFER, and I. G. KROOP. *American Heart Journal* [*Amer. Heart J.*] 48, 599–611, Oct., 1954. 4 figs., 18 refs.

It has been shown that if a dilute solution of the somatic polysaccharide isolated from the body of the pneumococcus is added to the serum of patients with pneumococcal pneumonia, a precipitate is formed. This reaction is also observed in rheumatic fever, subacute bacterial endocarditis, abscess of the lung, tuberculosis, congenital syphilis, and measles, but does not occur with normal serum. The reactive substance, C-reactive protein, migrates on electrophoresis with the α globulin, probably the α_1 fraction. C-reactive protein is nearly always found in the serum of patients with acute rheumatic fever, but is of no specific diagnostic value in differentiating this from other febrile states; it is, however, a sensitive index of rheumatic activity, disappearing with subsidence of this activity (usually before the fall in the erythrocyte sedimentation rate (E.S.R.)) and reappearing after the withdrawal of ACTH or cortisone therapy.

In the present study, which is reported from the Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, New York, the authors carried out the C-reactive protein test in 23 cases of acute rheumatic fever. They found the protein present in 9 out of 10 active cases and it disappeared in 6 out of 8 on the institution of cortisone and hydrocortisone therapy, the earliest disappearance of the protein being on the 8th day of treatment. In 12 out of the 18 cases tested after hormone therapy the test was positive, but in 8 of these subsequently became negative. The E.S.R. remained elevated one to 8 weeks after the protein had disappeared, but patients were allowed to get up provided the C-reactive test was negative. In 2 cases the result was negative in spite of rheumatic activity as evidenced by a raised E.S.R., tachycardia, and electrocardiographic changes. C-reactive protein was present in 2 patients with chorea and carditis, whereas it is always absent in uncomplicated chorea, which suggests that a positive result in chorea is indicative of the presence of carditis.

The authors conclude that the C-reactive protein test is a better guide to activity than the E.S.R., which may show protracted elevation despite an inactive clinical state. *F. Clifford Rose*

750. An Evaluation of Electrophoresis in Rheumatic Fever

I. G. KROOP, E. T. HEFFER, and N. H. SHACKMAN. *American Heart Journal* [*Amer. Heart J.*] 48, 612–623, Oct., 1954. 19 refs.

Fractionation of the plasma proteins by salting-out techniques has not shown any consistent diagnostic pattern in rheumatic fever, although reversal of the albumin:globulin ratio may occur. The plasma fibrinogen content may be elevated, particularly during the acute phase of the disease, but electrophoretic studies have not established a characteristic diagnostic pattern. The present authors have employed free solution electrophoresis, together with estimation of the erythrocyte sedimentation rate, blood fibrinogen level, and the protein flocculation and C-reactive protein tests, to determine the presence of rheumatic activity, a total of 40 electrophoretic determinations on 36 patients being carried out.

Decrease of the albumin fraction with reversal of the albumin:globulin ratio was the most frequent finding. The γ-globulin fraction was increased in most cases of

active rheumatic fever, irrespective of whether there was a preceding respiratory infection. The β-globulin fraction was increased in 7 out of 30 patients with rheumatic fever, and in 2 this was the only electrophoretic abnormality; the levels of the α_1 and α_2 globulins were elevated in active cases, and in some remained high despite cessation of rheumatic activity. Increase in the α_2-globulin fraction was frequently associated with non-rheumatic inflammation.

It is concluded that since a normal electrophoretogram may be obtained in the presence of rheumatic activity, and since abnormalities are found when the condition is clinically inactive, electrophoresis is of little value in determining the presence of rheumatic activity, although such activity is strongly suggested by a high β-globulin level. *F. Clifford Rose*

751. **Abortive Rheumatic Fever.** (Die abortive Polyarthritis rheumatica acuta)
H. J. Leu. *Praxis* [*Praxis*] **43**, 913–917, Oct. 28, 1954. 25 refs.

It is suggested by the author that rheumatic fever is frequently met with nowadays in an atypical and less florid form, and that more attention should be paid to abortive cases. The change in the nature of the disease is ascribed to mutations in the streptococcal population as a result of the widespread use of antibiotics.

Ten cases of the abortive form were noted in the course of one year (mainly in the spring) at the Swiss Military Hospital at Novaggio in apparently healthy recruits aged between 20 and 23. Single or multiple joints became painful and swollen, but the body temperature was not raised and the erythrocyte sedimentation rate (E.S.R.) was increased in only a few cases. Serum antistreptolysin titres were usually normal or slightly raised, and the agglutination reactions for haemolytic streptococci were negative in all cases. There was no anaemia, no leucocytosis, and no lymphocytosis or shift to the left. Clinically, there was no evidence of endocardial damage and there was no electrocardiographic evidence of myocarditis. *X*-ray films of affected joints were normal. Salicylates gave dramatic results. All 10 patients had chronic tonsillitis, and tonsillectomy was performed on 9 of them with excellent results—residual joint pain rapidly disappeared, the E.S.R. (where raised) fell to normal, and any albuminuria present cleared quickly.

The author discusses the classification of the collagen diseases and the differential diagnosis of his 10 cases.
D. Preiskel

752. **Isotopic Uric Acid in Gouty and Rheumatoid Arthritis Patients Treated with Probenicid and Phenylbutazone**
C. Bishop, A. Beyer, and J. H. Talbott. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 760–762, Aug.–Sept., 1954. 6 refs.

In investigations carried out at Buffalo General Hospital (University of Buffalo Medical School), New York, the size of the body's uric acid pool and its rate of turnover were studied in patients with gout or rheumatoid arthritis. After a control period probenicid was given in doses of 1·5 g. daily for a week, followed by phenylbutazone, 400 mg. a day, for a further week. With both drugs 2 patients suffering from rheumatoid arthritis showed a reduction in the size of the uric acid pool and an increase in the rate of turnover, but no increase in the urinary output of uric acid, whereas in 3 patients with gout and another with rheumatoid arthritis, in all of whom the serum uric acid level was abnormally high, there was an increase in uric acid output and again some reduction in the uric acid pool. The effect of probenicid seemed to be greater than that of phenylbutazone.
G. Loewi

753. **Hyaluronidase Therapy of Inflammatory and Degenerative Joint Diseases**
P. Rössing and H. Lutterbeck. *Rheumatism* [*Rheumatism*] **10**, 76–84, Oct., 1954. Bibliography.

A critical evaluation of the relationship of the hyaluronidase–hyaluronic-acid system to rheumatic disease of the joints led the authors to try local subcutaneous injection of hyaluronidase in the treatment of inflammatory and degenerative diseases of the joints, the rationale being the utilization of the absorption-promoting properties of hyaluronidase to remove the joint swelling. In a variety of cases of rheumatic joint disease 5 to 10 units of a hyaluronidase preparation, "kinetin", was injected subcutaneously "every 2nd to 4th day in the neighbourhood of the affected joints". The dosage was kept low because a higher one commonly produced inflammatory reactions. In 53 out of 83 cases there was definite subjective and objective improvement; in 14 cases no objective effect was observed, although some of the patients asserted that they were improved. Only one patient was apparently worse after this method of treatment. Degenerative diseases responded in the most satisfactory manner, as also did the groups of diseases designated "acute infective" and "toxic–allergic rheumatoid" arthritis. Results in rheumatoid arthritis were variable and bore no relationship to the state of activity of the disease. In rheumatic fever the results were less impressive. Later this treatment was combined with the depolymerizing effect of short-wave irradiation, with an improvement in the results. Intra-articular injection, which was tried on several occasions, proved painful and gave no better results than subcutaneous injection. Negligible skin reactions were observed at the site of injection on only 15 out of 800 occasions.

The authors incline to the view that a disturbance in the anabolism or catabolism of hyaluronic acid is the essential aetiological factor in inflammatory and degenerative diseases of the joints. Hyaluronic acid is present in increasing amounts in the joints of rheumatic subjects "although of a lower degree of polymerization". They do not support the view that increased activity of hyaluronidase is an essential component in the pathogenesis; furthermore they find that an increase in the serum level of antihyaluronidase [and of a number of other serum enzyme inhibitors] is a manifestation common to all inflammations and is not specific for rheumatism.
Harry Coke

Physical Medicine

754. **Value of Mechanical Aids in the Management of a Patient with Poliomyelitis**
G. J. Beck and A. L. Barach. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 1081–1094, June, 1954. 6 figs., 13 refs.

In this paper from the College of Physicians and Surgeons, Columbia University, New York, the authors describe three methods which may be utilized to aid breathing and expectoration in patients with bulbar poliomyelitis. A case report to illustrate the practical application of these methods is appended.

The first method is exsufflation with negative pressure. This consists in inflation of the lungs by a motor-driven blower to a pressure of 20 to 40 mm. Hg in 1 to 2 seconds, followed by a sudden release of pressure to 40 mm. Hg below atmospheric pressure, resulting in a high expiratory flow rate which will remove any mucopurulent plugs from the lungs. [The method was more fully described in the authors' previous paper (*Arch. intern. Med.*, 1954, **93**, 825; *Abstracts of World Medicine*, 1954, **16**, 484).]

The second method, involving respiration with the lungs immobilized, employs changes in air density for ventilation. A pressure chamber surrounds the entire body and the pressure is changed 25 times each minute from a positive pressure of 55 mm. Hg to a negative pressure of 55 mm. Hg, this producing an average tidal volume of 400 ml. There is no movement of the lungs.

The third method is the rocking bed. This device acts by tilting the patient head-down and feet-down alternately and produces inflation and deflation of the lungs by movement of the abdominal contents in relation to the diaphragm. In addition to these methods the effort of breathing can be assisted by the application of an "emphysema belt" to the abdomen; this lowers the respiratory rate and increases the tidal air, with no change in the arterial oxygen saturation, pCO_2, or *p*H. The authors state that the method of exsufflation with negative pressure may be a life-saving measure and that the other methods described enable the patient to breathe with less effort and more mental relaxation.

J. B. Millard

755. **The Use and Abuse of Physical Treatment in Industrial Medicine**
L. T. Wedlick. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 704–707, Oct. 30, 1954. 2 refs.

756. **Pain in the Neck. Based on a Study of 100 Cases**
M. Hart. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 90–94, July, 1954.

In discussing the results of treatment of 100 cases of pain in the neck at the Middlesex Hospital, London, the author stresses the value of obtaining a complete history which should include details of the social, personal, and family background, as in these cases a knowledge of the patient's personality is important. In all cases a routine general medical examination was carried out and also a detailed examination of the head, neck, shoulders, and upper limbs. The range of neck movements, pain on movement, and the distribution of referred pain were recorded. A routine radiological examination was also performed.

Of the 100 cases studied, 29 had solely organic lesions such as degenerative joint disease or a cervical-disk lesion to account for the symptoms; in 22 cases there was in addition a functional disturbance, such as chronic anxiety, cancerphobia, or a menopausal syndrome; the remaining 49 cases were considered to be suffering from a wholly functional condition. It was noted that in general a history of short duration was associated with an organic lesion and one of long duration with a psychopathological lesion. The radiological findings were not diagnostic, but pathological changes were seen in 90% of cases with solely organic lesions and in 63% of cases with a purely functional lesion.

The author makes some general observations on treatment, suggesting short-wave diathermy for degenerative joint disease and the administration of analgesics and conservative treatment for cervical-disk lesions. In degenerative joint conditions active neck exercises should be avoided as they tend to aggravate the symptoms, and in these cases some limitation of movement may have to be accepted. Psychogenic pain should be treated by the prolonged-interview technique of psychotherapy at monthly intervals, but the results are poor on the whole.

J. B. Millard

757. **Hyaluronidase in the Treatment of Acute Sprained Ankle. A Preliminary Report**
P. H. Kendall. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 95–97, July, 1954. 3 refs.

In the Department of Physical Medicine of Guy's Hospital, London, 119 cases of acute sprained ankle were treated, the following methods being used: (1) in 27 cases 1,000 units of "hyalase" (hyaluronidase) in 5 ml. of saline was injected into the area of effusion, and a supportive crepe bandage applied; (2) 17 cases were treated by surged faradism, effleurage, and exercises; (3) 25 cases were given a local injection of 2% procaine; (4) in 25 cases the ankle was immobilized in adhesive strapping; and (5) 25 cases received no treatment. The patients were examined daily and were regarded as being fully recovered if they had no pain, no swelling, and a normal gait.

The recovery times were: Group 1, 3·1 days; Group 2, 8·7 days; Group 3, 9·0 days; Group 4, 12·3 days; and Group 5, 13·9 days. The author stresses that treatment with hyaluronidase was obviously greatly superior to the other treatments, but that it should not be used if a haematoma is present.

J. B. Millard

Neurology and Neurosurgery

758. **"Mestinon" in the Treatment of Myasthenia Gravis**
M. R. WESTERBERG and K. R. MAGEE. *Neurology* [*Neurology*] **4**, 762–772, Oct., 1954. 16 refs.

"Mestinon" is an analogue of neostigmine; its anticurare effect is about one-half to one-quarter that of neostigmine, but its toxic effect is only about one-fifth.

In this report from the University Hospital, Ann Arbor, Michigan, detailed case notes of 22 patients with myasthenia gravis are given in order to illustrate their response to change from treatment with neostigmine to that with mestinon; the period of observation ranged from 3 to 7 months. All but one of the patients preferred mestinon to neostigmine; 15 found it gave them greater strength, 5 that it was about equal to neostigmine in this respect, while 2 thought it gave them less strength, but all were agreed that the effect of mestinon lasted longer. The most important difference to the majority of patients, however, was the maintenance of their strength on an even level without the necessity of frequent rest periods to gain strength, which they had found necessary while taking neostigmine. The authors consider that the sense of greater strength experienced by the patients was due either to the feeling of greater stability or to the patients being able to take longer courses of mestinon because of greater tolerance to it. One outstanding advantage of the new drug was the mildness, or in many cases the entire absence, of side-effects. *N. S. Alcock*

759. **Huntington's Chorea in Northamptonshire**
M. J. PLEYDELL. *British Medical Journal* [*Brit. med. J.*] **2**, 1121–1128, Nov. 13, 1954. 8 figs., 15 refs,

In an attempt to assess the incidence of Huntington's chorea in England and Wales, the author obtained records of 6 families with a history of the disease in response to a questionary sent to the general practitioners of Northamptonshire, while in addition information was obtained from the relatives of 2 certified patients with Huntington's chorea who had been admitted to the county mental hospital from the county area. Most of the familes concerned fell within the Registrar-General's Group IV (semi-skilled workers). By tracing back the pedigrees of these 8 familes, 61 cases of the disease were revealed, 13 of the patients being still alive in the county, among a population of approximately 263,000. These findings suggest that there may be more than 2,000 cases of Huntington's chorea in England and Wales.

Twelve patients exhibited athetoid movements, while the remaining patient suffered from mental deterioration, spasticity, a festinating gait, and other manifestations which characterized the disease in his family. Procainamide was administered to 6 patients with gross movements, but the treatment failed to exert any beneficial effect. Serological tests and electroencephalography produced no significant evidence bearing on either diagnosis or inheritance.

Although domiciliary care is obviously preferable to institutional supervision, the patient's antisocial behaviour frequently renders adequate control difficult, such control being all the more important since cortical degeneration results in heightened sexual interest and fecundity. So far as prevention of the disease is concerned the hereditary nature of the defect should be made clear to the offspring of an affected parent and they should be advised not to have children, while the question of termination of pregnancy may arise when one of the parents comes from an affected family or is suffering from the disease. It would be helpful if medical practitioners were to report the occurrence of cases of Huntington's chorea to the local health authority, the medical officer of health being in a better position to investigate family pedigrees and give appropriate advice to all branches of the family in an attempt to reduce the incidence of the disease. *A. Garland*

760. **The Significance of the Unilateral Argyll Robertson Pupil. Part II. A Critical Review of the Theories of Its Pathogenesis**
J. T. APTER. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **38**, 209–222, Aug., 1954. 2 figs., bibliography.

In this comprehensive review of the literature dealing with the pathogenesis of the Argyll Robertson pupil, presented from the Northwestern University School of Medicine, Chicago, the author points out that the inability of experimental lesions in the central nervous system to produce a pupil which is permanently miotic as well as inactive to light, the failure to demonstrate such a lesion histologically in the central nervous system of patients with neurosyphilis, and the difficulty of explaining the miosis of a unilateral Argyll Robertson pupil all combine in pointing to the conclusion that the causative lesion must lie outside the central nervous system.

Strong evidence in favour of an iridopathogenesis as advanced by Langworthy and Ortega (*Medicine*, 1943, **22**, 287) is provided by the reported results of clinical and histological examinations which have shown the presence of an abnormal iris in every case presenting the Argyll Robertson syndrome, by the finding of a colloidal-gold concentration curve in the aqueous humour of a paretic patient with Argyll Robertson pupils similar to that in the spinal fluid of neurosyphilitic patients, and by the high incidence of unilateral Argyll Robertson pupil (13 out of 46 cases of neurosyphilis) previously reported by the present author (*Amer. J. Ophthal.*, 1954, **38**, 34). In her opinion such a high incidence is incompatible with a pathogenesis based on a lesion in the central nervous system.

Summing up these various findings the author postulates that in neurosyphilis the blood vessels of the iris undergo the same pathological changes as the vessels in the dorsal nerve roots and optic nerve, with a partial occlusion and consequent undernourishment of the tissues, and this, by causing the nerves of the iris to atrophy, results in a small, immobile pupil. The overactive response of the Argyll Robertson pupil to accommodation is explained on the basis of the Helmholtz theory of normal accommodation. When the ciliary body contracts, the forward movement of the root of the iris causes the whole iris to move centripetally, resulting in constriction of the pupil which is purely mechanical in origin.

Edward Lyons

BRAIN AND MENINGES

761. **Directional Preponderance of Caloric Nystagmus in Patients with Organic Brain Disease. An Electroencephalographic Study.** [In English]
L. KIRSTEIN and L. PREBER. *Acta oto-laryngologica* [*Acta oto-laryng. (Stockh.)*] **44**, 265–273, May–June, 1954. 3 figs., 9 refs.

In 67 cases of cerebral or nervous disorder investigated by electroencephalography (EEG) at Södersjukhuset, Stockholm, the site of the EEG abnormality was studied in relation to the side of directional preponderance of nystagmus induced by the caloric method in order to determine whether electroencephalography is of value in locating the brain lesion.

A directional preponderance was found in 29 cases, and the EEG showed a focal abnormality in 25 cases, focal abnormal waves being recorded from the frontal, temporal, or parieto-occipital regions. In 8 cases giving a normal caloric response, abnormal EEG waves were recorded from the frontal or temporal region. The authors conclude that the finding of directional preponderance of nystagmus is not alone a certain sign of cerebral disease on the side of preponderance, but that when it occurs in combination with an EEG abnormality on the same side in cases in which other signs of cortical damage are absent, the evidence of a lesion in the cortex on that side may be considered to be strong.

William McKenzie

762. **Collateral Ophthalmic Artery Circulation in Thrombotic Carotid Occlusion**
K. VAERNET. *Neurology* [*Neurology*] **4**, 605–611, Aug., 1954. 3 figs., 8 refs.

In view of the rarity of cases in which it has been possible to demonstrate by arteriography functionally significant anastomoses between the extracranial and the intracranial arterial systems, the author, from the City Hospital and University of Aarhus, Denmark, describes his findings in 4 cases of thrombosis of the internal carotid artery in the neck in which arteriography was carried out.

The arteriograms showed that there may be anastomoses between the terminal branches of the ophthalmic artery and the external carotid artery. This, it is suggested, may account for the observed variability in both the severity and the duration of paralysis following thrombosis of the internal carotid artery, and indicates the need for restraint in the use of ligation of the external carotid artery, which has sometimes been advocated in the treatment of internal carotid thrombosis.

Hugh Garland

763. **Clinical Differential Diagnosis of the Minor Seizure**
H. C. GREGG and A. S. ROSE. *Neurology* [*Neurology*] **4**, 599–604, Aug., 1954. 1 fig., 6 refs.

An attempt was made at the University of California and the Veterans Administration Medical Center, Los Angeles, to differentiate the true petit mal seizure from the brief psychomotor seizure. Of 100 epileptic patients aged 22 to 67, psychomotor attacks occurred in 71, being transient in 58. Each patient was subjected to frequent examination and many attacks were observed.

In the authors' view brief seizures are frequently mistaken for petit mal seizures, and they suggest certain criteria for the differential diagnosis. They first emphasize that petit mal does not begin after the age of 20, whereas psychomotor epilepsy may occur at any age, although it is primarily a disorder of adults. Psychiatric disturbances are uncommon in association with petit mal, but are frequently observed in psychomotor epilepsy; the so-called "epileptic personality" is probably the personality of the patient who suffers from psychomotor attacks. An aura does not occur with petit mal, but is often an accompaniment of psychomotor seizures. In the petit mal seizure the patient is usually immobile, whereas in the psychomotor attack movement is the rule and incontinence is not infrequent. Recovery from petit mal is immediate, but after a psychomotor seizure the patient is confused for a minute or two.

The authors have found that electroencephalography is of the greatest value in the differential diagnosis of these two conditions.

Hugh Garland

764. **Surgical Occlusion of the Anterior Choroidal Artery in Parkinsonism**
I. S. COOPER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 207–219, Aug., 1954. 10 figs., 9 refs.

After the accidental tearing of the anterior choroidal artery during an attempted (but not effected) pedunculotomy on a patient with Parkinson's disease the author noted that tremor and rigidity had disappeared from the contralateral limbs. This led him to carry out the deliberate occlusion of this vessel, which supplies (among other structures) the globus pallidus and ansa lenticularis, in a series of 30 patients at New York University–Bellevue Medical Center. The operation was offered only to those patients with far-advanced Parkinsonism producing total incapacitation and resistant to all known methods of conservative therapy. Experience has led him to exclude cases of the arteriosclerotic type, the more recently treated patients therefore being all under 60 and their disease being of the post-encephalitic or idiopathic type.

The operation is now performed through a small temporal craniotomy. The temporal lobe is elevated

and the interpeduncular cistern opened. The posterior communicating branch of the internal carotid artery is seen, with the anterior choroidal artery above it. The latter is obliterated close to its origin, and it is stressed that at least 1 cm. of the vessel must be destroyed in order to prevent a collateral circulation developing from anastomoses between the anterior and posterior choroidal arteries over the lateral geniculate body. Careful postoperative nursing care is essential.

The mortality for the whole series was 13·3% (4 deaths), but there has been no mortality in the last 10 cases. There were 2 cases of postoperative hemiplegia and 3 cases of transient oculomotor palsy. Patients with postencephalitic Parkinsonism obtained more benefit than those with the idiopathic type, resting tremor being lessened or abolished in 9 out of 11 of the former. Rigidity was greatly benefited, this being the most striking effect of the operation, with a great reduction of incapacity and improvement in speech, swallowing, and automatic movements. Since, in uncomplicated cases, this operation is followed by no loss of power, it is to be hoped that further study will confirm the immediate postoperative results and demonstrate that the benefits are lasting. *J. E. A. O'Connell*

SPINAL CORD

765. **Effects of Intrathecal Mephenesin in Paraplegia**
L. BERLIN. *Neurology* [*Neurology*] **4**, 623–629, Aug., 1954. 4 figs., 10 refs.

The effect of intrathecal injection of a 2% solution of mephenesin in 6 adult males suffering from severe spastic paraplegia with involuntary flexor spasms of the legs was studied at the Veterans Administration Hospital, Bronx, and Cornell Medical College, New York. It was found that even 3 ml. reduced spasm and abolished clonus and deep tendon reflexes, but at the same time reduced voluntary movement in the legs. After injection of 10 to 15 ml. reflex and voluntary movements returned in about 2 hours, although there was a residual depression for some days. An elevation in the pain threshold, which was sustained for several days, was also noted. After repeated injections there was evidence of adhesive arachnoiditis, but it is nevertheless considered that intrathecal injection of mephenesin has some place in the relief of contractures and painful involuntary flexor spasms in irreversible paraplegia. *Hugh Garland*

766. **Cervical Spondylosis**
RUSSELL BRAIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 439–446, Sept., 1954. 2 refs.

In this discussion of cervical spondylosis, a condition which may lead to much disability, the author points out that the three main sites of cervical-disk protrusion are dorsomedial, dorsolateral, and intraforaminal, and that this protrusion is of two aetiologically distinct types, namely, nuclear herniation and annular protrusion; the former constitutes a fairly acute problem, but may in some cases, through degeneration or spondylosis, lead to the latter. The main factor is age, the attendant loss of elasticity and dehydration of the intervertebral disks causing additional wear and tear on the adjoining vertebrae and thus leading to osteophyte formation, the very mobility of the cervical spine contributing to this sequence of events. To this must be added the contributory effect of trauma in some 20 to 30% of cases.

The neurological effects of this osteochondral change may be upon the nerve roots, the cord, or on both. To some extent direct pressure is responsible, but indirect vascular effects—especially compression of the anterior spinal artery—play a part, and the intrinsic arterial disease in elderly patients may also have some influence. The effects of these factors may be increased by trauma, particularly forcible neck extension, and so produce in the cord a picture of myelomalacia. The symptomatology in the radicular cases comprises those of a brachial neuritis with certain additional features; thus, acroparaesthesiae and a picture resembling progressive muscular atrophy may be produced. The clinical results of damage to the cord are very variable; they are usually insidious, but with occasional acute exacerbations due to trauma, the chief symptoms being weakness of the lower limbs, numbness and clumsiness of the hands, radicular pain in the upper limbs, or variable wasting in the hands. The reflex and sensory changes vary with the level and the degree and duration of the compression. Dissociated anaesthesia may be encountered. In most cases the cerebrospinal fluid is normal, but occasionally its composition and dynamics may suggest an obstruction in the subarachnoid space. Radiography should be carried out in the erect, flexed, and extended positions, with antero-posterior and oblique views to show the foramina. Myelography may be necessary. It is stressed that radiographic evidence of spondylosis does not constitute proof of the fact that the neurological symptoms are due to this cause.

The differential diagnosis is often difficult since the condition may simulate motor neurone disease, disseminated sclerosis, subacute combined degeneration of the cord, or tumour, both intra- and extra-medullary; syringomyelia is rarely simulated. The course in cases of cord lesions is one of slow deterioration, finally becoming stationary and leaving the patient in most instances disabled but able to get about. As to treatment, immobilization of the neck for several months is advised, first in a plaster collar, then in a plastic one. The author has not been impressed with the value of head traction, and manipulation he considers to be dangerous. In general, surgery is most likely to be successful when the patient is relatively young, the history short, the disk protrusion single rather than multiple, and the cardiovascular system in good state. Decompression is favoured rather than an attempt to remove an arteriorly placed osteophyte. On the whole a conservative approach is considered best. *Fergus R. Ferguson*

767. **Motorized Intermittent Traction for Treatment of Herniated Cervical Disk**
H. A. SHENKIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1067–1070, Nov. 13, 1954. 4 figs., 2 refs.

Psychiatry

768. **Schizasthenia (Dimitrijevic).** (La schizastenia di D. T. Dimitrijevic)
A. SANGUINETTI. *Giornale di psichiatria e di neuropatologia* [*G. Psichiat. Neuropat.*] **82**, 285–305, 1954. Bibliography.

After reviewing the difficulties inherent in the present classification of the various types of schizophrenia, the author discusses Dimitrijevic's concept of "schizasthenia". This term is applied to certain mental conditions which are on the borderline between schizophrenia and the neuroses and which, in Dimitrijevic's opinion, constitute a particular and latent form of schizophrenia. The syndrome is characterized by prolonged and marked physical weakness, mental tiredness, and abnormal irritability, which renders the individual incapable of meeting the demands of his social environment. Schizasthenia may precede, accompany, or follow a clear-cut schizophrenic illness.

Schizasthenia differs from the neuroses in that the feeling of lassitude is more profound and is not amenable to suggestive therapy, while the irritability is more intense. Lack of interest, emotional indifference, and negativism may also be present. It is distinguished from schizophrenia by the predominance of asthenia and hypersensitivity over any dissociative manifestations.

The author reports 2 cases which he found difficult to diagnose along orthodox lines and which appear to conform to Dimitrijevic's definition of schizasthenia.

P. Cassar

769. **Leucotomy and Subcortical Lobotomy.** (Leucotomia e lobotomia sottocorticale)
A. GUERRA and C. SACCO. *Giornale di psichiatria e di neuropatologia* [*G. Psichiat. Neuropat.*] **82**, 317–335, 1954. 1 fig., 6 refs.

The authors describe and discuss the results of leucotomy and subcortical lobotomy in 27 cases of schizophrenia and other psychoses (17 in males and 10 in females) operated on since March, 1949, at the Udine Provincial Psychiatric Hospital, Italy. In the first 8 cases leucotomy according to the technique of Moniz was performed. These patients all had a long-standing illness marked by violent episodes and had responded only slightly to other forms of therapy. The results of leucotomy were also poor, and this induced the authors to modify their technique and to be more selective in their choice of patients. The technique they now use is that of subcortical lobotomy, which aims at cutting the cortical connexions at the junction of the grey and white matter. The operation, which is performed under local analgesia, is fully described, with illustrations of the instruments used. [For technical details the original paper should be consulted.] It is claimed that this technique is an improvement over that of Freeman and Watts in that it avoids the risk of injuring the vessels of the falx and lateral ventricles, prevents the occurrence of postoperative neurological and mental complications, and is safer. The presence of cerebral arteriosclerosis, cardio-renal insufficiency, organic senile changes, or a haemorrhagic diathesis is regarded as a contraindication to the operation.

In all patients subjected to this procedure there was a rise of temperature lasting a few days after the operation; 2 patients had incontinence of urine for the first 2 or 3 days, while another had a few epileptic fits. There was no case of paralysis, and no fatalities. Of the 19 patients, ranging in age from 26 to 55 years, who underwent the operation, 6 improved sufficiently to warrant their discharge from hospital, 2 had a temporary remission, and the condition of 2 others has improved, although they are still in hospital; the remaining 9 showed no improvement. On the whole, schizophrenics with retention of affect responded best to the operation, while those with a severe degree of dissociation derived the least benefit. The fundamental importance of postoperative psychotherapy and re-education is stressed. *P. Cassar*

770. **Cocarboxylase in the Treatment of Delirium Tremens and Other Acute Psychoses.** (La cocarbossilasi nella terapia del delirium tremens e di altre psicosi acute)
U. GALLIAN and G. GAMNA. *Giornale di psichiatria e di neuropatologia* [*G. Psichiat. Neuropat.*] **82**, 307–315, 1954. 30 refs.

Cocarboxylase (phosphorylated aneurin) plays a very important part in carbohydrate metabolism. Any defficiency, brought about by inadequate dietary intake or by increased metabolic demands, results in acidosis owing to abnormal accumulation of pyruvic acid and ketone bodies in the tissues.

The authors have therefore tried the effect of cocarboxylase in the treatment of certain acute psychoses which are associated with acidosis, 7 cases of alcoholic and 3 cases of puerperal confusional state being treated with 100 to 200 mg. a day for the whole duration of the acute manifestations. In the first few cases the drug was injected intramuscularly, but in subsequent cases it was given intravenously, the authors finding this route preferable. Four of the patients died, but the rest recovered, some of them within a few days. Although all the patients were given other drugs concurrently, such as antibiotics, vitamins, sedatives, and cardiac stimulants, the authors express themselves as satisfied that the results obtained can be attributed largely to the cocarboxylase.

P. Cassar

771. **A Study of the Immunology and Biology of Mongolism.** [In English]
M. DONNER. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **32**, Suppl. 9, 1–80, 1954. 5 figs., bibliography.

Dermatology

772. **Studies on the Therapeutic Effect of Trypsin**
B. HEILSEN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 7–15, July, 1954. 16 refs.

The author briefly discusses previous reports on the value of enzyme preparations in the treatment of lesions in which necrotic tissue is an obstacle to healing. At the Rudolph Bergh Hospital, Copenhagen, he has treated 36 patients with various types of leg ulcer, gangrene, and burns with 25 to 50 mg. of crystalline trypsin dissolved in Sorensen's phosphate buffer solution. The methods employed, the results obtained, and the occasional undesirable effects of the treatment are described.

Rapid removal of the necrotic tissue of the ulcers occurred in all cases. The author suggests that lesions in which there is insufficient vascularization, such as arteriosclerotic ulcers and gangrene, should be treated with smaller doses and less frequently. The treatment was particularly effective in varicose ulcers and diabetic gangrene. *G. B. Mitchell-Heggs*

773. **Cutaneous Porphyria in the Adult**
M. BOLGERT and J. CANIVET. *British Journal of Dermatology* [*Brit. J. Derm.*] **66**, 312–317, Aug.–Sept., 1954. 1 ref.

The authors, from the Hôpital Saint-Louis, Paris, describe a study of cutaneous porphyria based on 17 cases seen by them since 1951. This disease usually starts in early adult life, but may sometimes occur even in old age. The essential skin lesion consists in bullae appearing in groups on exposed healthy skin and sometimes surrounded by a narrow erythematous zone. Vesicles also occur. There are pruritus and tension. A crust forms, and eventually a round pigmented or, later, depigmented patch is left. Histologically the floor of the bulla presents a fringed appearance. The urine may be found to contain from 3·5 to 14 mg. of uroporphyrin; it is reddish-orange or pink in colour, the intensity of the colour varying during the day or night and during periods of remission. The disease occurs in attacks which always start in the spring or early summer, mainly under the influence of sunlight, and runs a benign course. A history of chronic alcoholism is common.
Kate Maunsell

774. **Cation-exchange Resins in the Treatment of Extensive Dermatoses, Particularly Eczema.** (Kationenaustauscher in der Behandlung von ausgebreiten Dermatosen, insbesondere Ekzemen)
G. BREHM and G. W. KORTING. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **130**, 743–748, 1954. 1 fig., 31 refs.

At the University Dermatological Clinic, Tübingen, an attempt was made to influence the progress of 16 cases of dermatosis in which oedema due to local water retention was an important feature by administering cation-exchange resins. The conditions so treated included cases of eczema, seborrhoeic eczema, seborrhoeic erythrodermia, and chronic urticaria. No benefit was noted.

As the action of these resins is primarily on the extracellular fluid at the periphery, the negative results obtained are thought to provide evidence that the nervous regulation of electrolyte and water balance in skin disorders of the eczema group is controlled centrally.
G. W. Csonka

775. **Trichostasis Spinulosa**
E. LADANY. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 33–41, July, 1954. 2 figs., 27 refs.

Since 1901, when it was first described by Franke, only some 200 cases of trichostasis spinulosa have been reported in the literature. This condition, which is probably more common than has been thought, is a peculiar follicular disorder characterized by the appearance of protruding plugs in groups of hair follicles; microscopical examination of these plugs shows them to consist of from 10 to 45 lanugo hairs embedded in a horny mass. In the present paper the clinical features and pathology of 7 cases of trichostasis spinulosa are described, and the aetiology and pathogenesis discussed. Comparative studies of this condition and of comedones suggest that trichostasis spinulosa is a variant of comedones, although it has a sufficiently distinctive character to be considered as a separate entity.
G. B. Mitchell-Heggs

776. **The Dilated Pore, a Trichoepithelioma**
L. H. WINER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 181–188, Sept., 1954. 5 figs., 4 refs.

The treatment of the solitary enlarged pore has not hitherto been very satisfactory. With a view to gaining a better understanding of this abnormality the author, working at the Veterans Hospital, Sawtelle, California, has performed excision biopsy by means of a cutaneous punch on 10 patients with solitary enlarged pores of the face.

The microscopical appearances of serial sections are described in detail and discussed in relation to similar appearances in other conditions. The author states that without a knowledge of the clinical history the histological appearances could be confused with those of seborrhoeic keratosis, cylindroma, epithelioma adenoides cysticum, basal-cell carcinoma, and even intermediate-cell carcinoma. He concludes that the dilated pore is a secondary or acquired trichoepithelioma, and suggests that it is best treated by excision at least 2 mm. beyond its ostium after first having expressed the keratin contents. Because of its depth in the cutis, it is clear that no merely superficial measures such as have often been employed could eradicate this lesion. *G. B. Mitchell-Heggs*

Paediatrics

777. **Newer Therapeutic Procedures Designed to Prevent Abnormal Pulmonary Ventilation in the Newborn Infant**

A. BLOXSOM. *Journal of Pediatrics* [*J. Pediat.*] **45**, 373–392, Oct., 1954. 17 refs.

As a means of reducing neonatal mortality the author advocates, among other things, the use of an " air lock " of his own design in the resuscitation of the newborn infant. [The air lock is not described in this paper, but it appears to be an apparatus in which the infant is placed in an atmosphere of 60% oxygen and in which the pressure is raised and lowered once every 40 to 60 seconds, on the principle of Thünberg's " barospirator ".] He discusses the changes which take place in the alveolar lining of the lung following birth, and suggests that the cytoplasm of the cuboidal epithelial cells of the foetal lung is rendered plastic through the imbibition of fluid, so that at birth, or shortly before, a change can take place as a result of the stimulus of pressure changes during labour or respiratory movements after delivery, whereby the cells are flattened to line the alveoli completely. The epithelial cells of the premature infant are insufficiently mature and plastic to undergo this " metamorphosis ", while the infant born by Caesarean section lacks the stimulus of pressure changes *in utero*. It is also suggested that " the intracellular binding cement (hyaluronic acid) also may hinder progressive expansion of the pulmonary alveoli and the separation of the squamous alveolar cells of some infants to provide functioning alveolar sacs ", while tenacious mucus in the lungs may further prevent proper expansion.

The author therefore recommends the following principles of treatment for the newborn infant. (1) Accessory barospiration in his air lock, which provides a high concentration of oxygen during the stage of " metamorphosis ", and hastens the latter by pressure changes. (2) Administration of nebulized hyaluronidase solution to permit more rapid expansion of the alveoli. Thus " the lungs are expanded in a colloidal water–oxygen–air therapeutic-sized mist system for a sufficiently long period to prevent a possible reabsorption atelectasis." (3) Administration by nebulization of a detergent (" triton A-20 ") to liquefy tenacious mucus, and penicillin to prevent infection.

It is claimed that as a result of the introduction of these measures at St. Joseph's Maternity Hospital, Houston, Texas, the death rate per 10,000 full-term deliveries fell from 63 to 37 and the death rate per 10,000 premature births from 2,228 to 1,504 between the years 1949 and 1952.

(In view of the controversial statements made in this paper it was submitted, with the author's consent, to a panel of 10 physiologists, pathologists, obstetricians, and paediatricians, 5 of whom were nominated by the Editor of the *Journal of Pediatrics* and 5 by the author himself, and their comments are published here. Of the 10, 7 (Wilson, Whittenberger, Barach, Smith, Virginia Apgar, Edith Potter, and Gruenwald) find the theoretical basis put forward by the author for his treatment unacceptable in greater or less degree, and point out numerous flaws in his argument. From the statistician's point of view, Weech points out that although the improvement in neonatal mortality reported is unlikely to be fortuitous, no data are provided concerning factors other than the use of the air lock which may have affected mortality. Eastman states that he is carrying out a controlled experiment with the air lock, and is not yet prepared to express an opinion as to the value of the apparatus, but Miller states that he has had good results with the air lock in certain types of case. He also suggests that the difficulties of the newborn period are so great and the therapeutic tools available so few that each new approach should be judged by its clinical usefulness without wasting time in quibbling about its theoretical basis.)

I. A. B. Cathie

778. **A Study of Hemograms in Premature Infants**

G. G. HADLEY and R. F. CHINNOCK. *Journal of Pediatrics* [*J. Pediat.*] **45**, 413–418, Oct., 1954. 5 figs., 2 refs.

At the County Hospital, Los Angeles, California, the "haemogram", as represented by the erythrocyte count, haemoglobin value, packed cell volume, and total and differential leucocyte counts, was determined by the authors in respect of 117 premature infants weighing 1,600 g. or less at birth. They found that the haemoglobin value fell after birth until about the 9th week, and that in general the smaller the birth weight, the greater was the fall. Similar observations were made with regard to the erythrocyte count and packed cell volume, and it was noted that the mean size of individual erythrocytes was diminished. From these results absolute values were calculated. It is pointed out that the so-called " anaemia of prematurity " is characterized by the small size as well as small numbers of erythrocytes and not by reduced concentration of haemoglobin within the cells, so that the anaemia is normochromic rather than hypochromic. [No references are made to other work in this field.]

I. A .B. Cathie

779. **Oxygen and Retrolental Fibroplasia. A Seven-year Survey**

R. M. FORRESTER, E. JEFFERSON, and W. J. NAUNTON. *Lancet* [*Lancet*] **2**, 258–260, Aug. 7, 1954. 2 figs., 5 refs.

Among 899 premature infants admitted to St. Mary's Hospital and the Duchess of York Hospital for Babies, Manchester, between 1947 and 1953, there were 83 cases of retrolental fibroplasia. Ocular damage was permanent in 36 infants, causing blindness in 21 of these. The incidence of the disease was highest in 1950 and 1951 —years in which high concentrations of oxygen were given intensively to the premature infants in both

hospitals. From the autumn of 1951 the amount of oxygen given to each infant was greatly reduced and the duration of administration to each infant fell progressively from an average of 8 or 9 days to less than 24 hours. No further cases of blindness occurred after that year, and no permanent eye changes were detected among infants born in the last 18 months of the period under review. The reduction in the amount of oxygen had no demonstrable adverse effect on the mortality among premature babies.

The 899 infants here considered include 629 previously reported by one of the authors (Jefferson, *Arch. Dis. Childh.*, 1952, **27**, 329; *Abstracts of World Medicine*, 1953, **13**, 160) to which the present authors have added 270 survivors among those admitted during the period 1952–3 and adequately followed up for at least 6 months. The proportion of those followed up was thus 95%—270 out of 284. *Mark S. Fraser*

780. **Recovery from Meconium Peritonitis**
J. F. R. BENTLEY and D. J. WATERSTON. *Lancet* [*Lancet*] **2**, 990–992, Nov. 13, 1954. 14 refs.

781. **Prolonged Obstructive Jaundice in Infancy. IV. Neonatal Hepatitis**
S. S. GELLIS, J. M. CRAIG, and D. Y. Y. HSIA. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 285–293, Sept., 1954. 27 refs.

Of a series of cases of prolonged obstructive jaundice in infancy admitted to the Children's Medical Center (Harvard Medical School), Boston, the authors considered 42 to have the syndrome of inspissated bile unassociated with erythroblastosis foetalis, atresia of the bile ducts having been excluded by laparotomy or by clinical recovery. A follow-up 6 months to 12 years after recovery showed 29 (71%) to be alive, well, and clinically normal; 4 were alive but jaundiced, with cirrhosis and portal hypertension; 8 (19%) had died jaundiced, one after operation and the rest 2 months to 2 years later from bleeding oesophageal varices and liver failure; and one patient could not be traced. On re-examination of sections of the liver from these cases, all were found to have the changes described by Craig and Landing as diagnostic of viral hepatitis. A questionary was sent to each family inquiring about other cases of jaundice in infancy or in the mother during pregnancy, but jaundice was reported in only one mother, in none of the 25 older siblings, and in only one of the 7 younger siblings of the propositi. The authors describe this last case and report 2 other cases, from different sources, of neonatal hepatitis occurring among siblings.

In discussing aetiology the authors conclude that if neonatal hepatitis is viral in origin, the virus is more likely to be that of homologous serum jaundice than that of infective hepatitis, although it is possible that some virus other than these two may eventually be incriminated. Surgery should be avoided as being badly tolerated by affected infants. Oral cortisone is useful in diagnosis, having no effect on obstructive jaundice whereas it lowers the serum bilirubin level and relieves the obstruction in hepatitis. They suggest the administration of gamma globulin to the mothers of affected infants in doses of 0·1 ml. per lb. (0·22 ml. per kg.) body weight intramuscularly every 6 to 8 weeks during any subsequent pregnancy. *A. W. Franklin*

782. **The Study of Hypothyroidism in Childhood Using Radioactive Iodine.** [In English]
J. H. HUTCHISON. *Maandschrift voor kindergeneeskunde* [*Maandschr. Kindergeneesk.*] **22**, 298–301, Sept., 1954. 16 refs.

The thyroid uptake, plasma concentration, and urinary excretion of radioactive iodine (^{131}I) in juvenile myxoedema was studied at the University and the Royal Infirmary, Glasgow. A dose of 30 to 200 μc. of ^{131}I was given to 13 children with hypothyroidism and some degree of thyroid gland enlargement. It was found that the thyroid gland was hyperactive in taking up iodine, binding it with protein, and discharging it into the circulation, but that there was a defect in the hormone production, the end-product being an unidentified thyroxine-like substance. Of these 13 children, 8 belonged to one family group in which there was considerable consanguineous mating. In 2 patients without enlargement of the thyroid gland the hypothyroidism was due to inadequacy of ectopic thyroid tissue in the absence of a normal thyroid gland. *R. Crawford*

783. **Intraspinal Tumors in Children**
H. J. SVIEN, E. P. THELEN, and H. M. KEITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 959–961, July 10, 1954. 1 fig.

Tumours of the spinal cord and its meninges are rare in childhood. Over a 20-year period at the Mayo Clinic only 41 cases of intraspinal tumour in children under 15 years were seen, 19 of the 41 patients being between 11 and 15 years of age. The sex incidence was not significant, 18 of the patients being boys and 23 girls. The neoplasm arose from the spinal cord itself or the meninges in 27 cases, the commonest types being neurofibroma (8 cases), lipoma (6 cases), glioma (8 cases, including 2 of intramedullary ependymoma and 2 of ependymoma of the filum terminale which are classified as gliomata). The tumours originated in adjacent tissue in 9 cases and were mostly highly malignant, arising as sarcomata from bone or soft tissue. In 2 cases there were tumours of the lymphoma type—a reticulum-cell sarcoma and a lymphoblastoma—and in 2 there were metastatic tumours, the primary tumour being a carcinoma of the thyroid in one case and "Ewing's" sarcoma of the sternum in the other.

The authors state that in 14 of the 41 cases "surgical removal of the tumour would result in a cure provided that the operation was performed before the tumour had caused irreparable damage to the spinal cord". In any case they recommend that if complete removal of the tumour is not possible, laminectomy, decompression, and partial removal should be attempted, as these operative procedures "sometimes result in prolonged benefit". [It is not clear from the article whether the operative procedures described as feasible were actually performed.] *Ruby O. Stern.*

Medical Genetics

784. **New Genealogical Tree of Granulomatous Corneal Dystrophy (Groenouw I).** (Nouvel arbre généalogique de dystrophie cornéenne granuleuse (Groenouw I)
J. B. BOURQUIN, J. BABEL, and D. KLEIN. *Journal de génétique humaine* [*J. Génét. hum.*] **3**, 137–146, Aug., 1954. 1 fig., 12 refs.

The authors present, from the University Ophthalmological Clinic, Geneva, the genealogical tree of a Swiss family afflicted with granulomatous corneal dystrophy. The family first came under observation in 1938, so that reasonably adequate information regarding affected members could be obtained only for the last 4 generations; the data include the findings for one branch of the family which emigrated to New Zealand and was reported by Hope-Robertson (*Trans. ophthal. Soc. N.Z.*, 1949, **3**, 71). The four successive generations investigated comprised 95 persons, of whom 54 showed signs of corneal dystrophy, an incidence of 58·8%. The disease has shown a regular dominant hereditary transmission with complete penetrance and a notable predominance of the affection among the women of the family, 36 out of 51 females being affected and only 18 out of 44 males. In most members examined the clinical picture has been more or less similar, and in nearly all cases the evolution has been slow and benign; one daughter underwent keratoplasty at the age of 38. However, in certain cases there were variations in the morphology and in the pattern of evolution of the disease; as a rule the variations were similar among persons belonging to the same branch of the family. *P. Sander*

785. **Familial Factor V Deficiency: the Pattern of Heredity**
C. S. KINGSLEY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 323–329, July, 1954. 3 figs., 23 refs.

The inheritance of a deficiency of Owren's Factor V (labile factor), which is necessary for the conversion of prothrombin to thrombin, has been studied by the author at the Institute of Pathology, Pretoria, in two probably related families, for one of which a full genealogical tree is given. In each family three types of individual could be recognized: (1) those with almost complete absence of Factor V, (2) those with partial deficiency of the factor, and (3) those with normal concentration of it. The individuals of Type 1 showed clinical evidence of the haemorrhagic diathesis (Owren's disease).

The familial distribution of the three types suggested that those individuals with complete absence of the factor were homozygous for a rare mutant gene. The individuals with a partial deficiency, who were otherwise quite healthy, appeared to be heterozygous for the abnormal gene; Factor-V activity in these heterozygotes was very variable and though it was usually about 40 to 60% of normal, values as low as 24% and as high as 68% of normal were found. It is concluded that the defective gene, although clinically recessive, nevertheless has a potency almost equal to its normal counterpart and the author suggests that cases may yet be encountered in these families in which the gene is either completely recessive or partially dominant. *Harry Harris*

786. **Two-generation Pyloric Stenosis**
C. O. CARTER and B. W. POWELL. *Lancet* [*Lancet*] **1**, 746–748, April 10, 1954. 12 figs., 16 refs.

Assessment of the incidence of infantile pyloric stenosis among the children of persons who were themselves affected in childhood or among the parents of index cases has hitherto been difficult in Great Britain, where the Rammstedt operation was not performed with any frequency until 1918, few cases of this condition being admitted to hospital before that time. The authors attempted to trace all the 358 individuals (299 male, 59 female) who survived operations for congenital pyloric stenosis performed between 1920 and 1929 at The Hospital for Sick Children and at St. Thomas's Hospital, London. Of the 85 traced, 22 men and 6 women had married and had offspring; 3 of their 25 sons and none of their 21 daughters had had pyloric stenosis requiring operation, while characteristic symptoms of pylorospasm were present in another son and 3 daughters.

The remaining 273 individuals could not be traced at their original address, but 6 sons and one daughter were known to have been treated by operation for the condition. The authors estimate the approximate number of children of these 273 individuals from the marriage and fertility tables derived from the 1% sample of the 1951 census, and thus obtain a conservative estimate of the incidence of pyloric stenosis among these children.

From these two series the incidence of pyloric stenosis requiring operation among the children of persons who themselves had the operation may be roughly estimated as 1 in 10 for sons and 1 in 50 for daughters, which is the same as the incidence among brothers and sisters of index cases as reported by other authors. It is suggested that the data so far available are consistent with the hypothesis that pyloric stenosis is transmitted as a dominant gene manifested in 1 in 5 boys and 1 in 25 girls of homozygous genotype. *R. H. Cawley*

787. **Familial Disseminated Sclerosis. Observations on Three Sisters with Histological Confirmation in One Case.** (La sclérose en plaques familiales. Observations de trois sœurs. Contrôle histologique d'un de ces cas)
R. AMYOT. *Presse médicale* [*Presse méd.*] **62**, 1347–1349, Oct. 6, 1954. 3 figs., 5 refs.

788. **Multiple Cretinism in a Family**
J. B. C. NABNEY. *Lancet* [*Lancet*] **2**, 1107, Nov. 27, 1954. 1 fig., 4 refs.

Public Health

789. **Influence of Birth Weight, Sex, and Plurality on Neonatal Loss in the United States**
S. SHAPIRO. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1142–1153, Sept., 1954. 2 figs., 9 refs.

This paper is based on information obtained from the birth records of the 837,786 infants born during the first 3 months of 1950 in the United States (excluding Massachusetts, where no record is made of birth weight or period of gestation), and from the death certificates of those of them who died within 4 weeks of birth. The birth-weight distribution is examined in relation to sex, race, plurality of birth, and gestation period, and neonatal mortality studied in relation to the same factors. The data are fully tabulated.

The modal birth-weight group was 3,001 to 3,500 g. for both males and females and for both white and coloured infants, but in general males weighed more than females and whites more than non-whites. Birth weights among the coloured population were more often at the extremes of the distribution (<2,500 g. or >4,500 g.) than among the white population. Less than 50% of individual members of plural sets (twins or triplets) weighed more than 2,500 g. at birth. Neonatal mortality decreased with increasing birth weight, the minimum being among infants weighing 3,501 to 4,000 g., and thereafter increased sharply. Two-thirds of the neonatal deaths were those of infants weighing 2,500 g. or less at birth. The neonatal mortality for whites was higher than that for non-whites when the birth weight was less than 2,000 g., and lower when it was over 2,750 g. The respective rates, standardized for birth-weight differences, were: white 19·6 per 1,000, coloured 22·6 per 1,000.

The neonatal mortality for multiple births was lower than that for single births where the birth weight was less than 2,500 g., and higher where it was over 3,000 g., 10% of the total neonatal deaths being associated with plural birth. The neonatal mortality among males was higher than that among females with respect to all birth weights up to 4,500 g. The association between mortality and birth weight was most marked for deaths occurring earlier in the neonatal period, and the mortality at less than 3 weeks of age was higher among whites than among non-whites. *R. H. Cawley*

790. **The Physique of Oxford Undergraduates. Relationship with Weight Variation, Schooling and Habits**
R. W. PARNELL. *Journal of Hygiene* [*J. Hyg. (Lond.)*] **52**, 369–378, Sept., 1954. 12 refs.

During the years 1947–50 the physique of men and women undergraduates was studied at the Institute of Social Medicine, Oxford, in relation to social class, pre-university schooling, Sheldonian somatotype, and (more especially for the study of weight variations) sporting and smoking habits. Comparison was made with similar groups in the general population and in American universities and, in some instances, with groups of Oxford undergraduates examined in previous years. Most of the subjects, apart from ex-servicemen, were under 20 years of age.

It was found that men coming from private and public schools were, on average, taller and heavier than those from government-aided schools, and that, as has been demonstrated in the general population, height and weight increased progressively with the social class as defined by the Registrar-General. However, the shortest and lightest undergraduate group was as tall as, and 9 lb. (4·1 kg.) heavier than, the tallest and heaviest group in the general population within the same age limits, while the Oxford students were substantially heavier and taller than American undergraduates of identical somatotype. These findings cannot be explained on a purely nutritional and economic basis and the author suggests that the factors determining the difference between the undergraduate and general population are probably of genetic origin. In support of this it is noted that, in spite of changes in the social status of undergraduates, their average weight and height is much the same now as it was in 1908–10, when Schuster studied the physique of 959 Oxford undergraduates.

During their first year loss of weight was commoner in women than in men, the most frequent cause apparently being psychological stress. Men from boarding schools and ex-servicemen gained weight less often than those from day schools, and men from private and public schools less often than those from elementary and secondary schools. Generally speaking, the evidence indicates that gain in weight is related to somatotype rather than environment. Similarly, such differences as were noted in weight change between smokers and non-smokers and between those who played games and those who did not can be best explained by differences in somatotype.

[As is to be expected in work coming from this source, this is a valuable piece of research clearly presented.]
R. J. Matthews

791. **Trial of Hexylresorcinol as Air Disinfectant for Prevention of Colds in Office Workers**
O. M. LIDWELL and R. E. O. WILLIAMS. *British Medical Journal* [*Brit. med. J.*] **2**, 959–961, Oct. 23, 1954. 1 fig., 7 refs.

During the winter of 1952–3 the authors carried out a carefully controlled trial of hexylresorcinol as an air disinfectant of rooms in a large office in Newcastle upon Tyne, each of which accommodated about 45 individuals. Some preliminary observations the previous winter had shown that the incidence of colds in 6 different rooms was very similar, and it was therefore decided that the conditions were suitable for a test of the value of hexyl-

resorcinol in reducing this incidence. The methods adopted in this investigation, which continued over a period of 38 weeks, are described at length, with details of the population studied and the way in which illnesses were recorded. Four vaporizers designed to yield 30 mg. of hexylresorcinol an hour were installed in each of 6 rooms, hexylresorcinol and an inert substance being dispensed from these over alternate periods. On 4 occasions during the winter samples of air were taken and examined bacteriologically.

The findings are analysed and results set out in 3 tables and a graph. There was no detectable difference between the incidence of colds in the treated rooms and that in the control rooms. The concentration of hexylresorcinol in the air was less than 1 μg. per cubic foot (35 μg. per c. metre), and was apparently insufficient to reduce its bacterial content. A further test showed that the bacterial content of the air could not be effectively lowered without risk of causing respiratory-tract irritation from the hexylresorcinol.

It is concluded that the addition of hexylresorcinol vapour to the air had no effect on the attack rate for the common cold and other similar affections, or on the absence rate. The authors are unable to explain the beneficial effects reported by other observers.

A. Trevor Jones

EPIDEMIOLOGY AND IMMUNIZATION

792. **Report on the Use of Gamma Globulin and Adult Serum for Measles Prophylaxis in England and Wales, 1949–53**

J. C. McDONALD and W. C. COCKBURN. *British Medical Journal* [*Brit. med. J.*] **2**, 1076–1079, Nov. 6, 1954. 13 refs.

Since 1949 the Central Health Laboratory, Colindale, has distributed gamma globulin (250 mg. dissolved in 3 ml. of sterile distilled water) and irradiated adult serum in normal strength and in threefold concentration for measles prophylaxis. All doctors using these prophylactics were asked to complete a standard form reporting the results obtained. During the period October, 1949, to December, 1953, report forms were returned for 82% of the 12,408 doses of globulin and 67% of the 3,931 doses of adult serum issued, the data being then analysed to obtain information concerning the distribution of measles prophylactics, and to determine the incidence of local and general reactions to inoculation and the influence of dosage and the period between exposure and inoculation on the prophylactic effect. Only reports (4,080 in number) relating to home contacts under 5 years of age were analysed to determine the prophylactic effect, and, in the absence of controls, the average attack rate in susceptible children calculated from published series was used for purposes of comparison.

In London and the south-east of England some 10 contacts were inoculated for every 1,000 cases notified, compared with about 3 per 1,000 in other regions. Of the gamma globulin issued, 60% was used in hospitals, most of it being given to children under 3 years of age. Moderate or severe local reactions were noted in 0·3% of children given gamma globulin, 1% of those given unconcentrated adult serum, and in 1·2% of those given concentrated adult serum. Moderate or severe general reactions were observed in 0·8% with gamma globulin and 1·4% with unconcentrated adult serum. No reaction was severe enough to cause anxiety.

A considerable reduction in the attack rate was achieved (as compared with the published findings of others) with less than 2 ml. of gamma globulin in children aged 6 months to one year, with 2 to 4 ml. in children between one and 3 years of age, and with 4 to 8 ml. in those between 3 and 5 years. The doses required to reduce the attack rate to about 25% were 2 to 4 ml. in children aged 6 months to one year, 4 to 8 ml. in children aged one to 3 years, and more than 8 ml. in those aged 3 to 5 years. The proportion of children under 5 years who developed measles after being given adult serum was little less than would have been expected had they not been treated. Delay between exposure and inoculation with gamma globulin did not appear to have any effect in children under one year of age, and in children between one and 3 years such effect was slight.

From the findings in this investigation the authors recommend that so long as the demand for gamma globulin exceeds supply the following dosage scheme should be followed:

Aim	Age of Child		
	Under 1 Year	Over 1 Year and Under 3 Years	Over 3 Years
Prevention ..	3 ml. (250 mg.)	6 ml. (500 mg.)	9 ml. (750 mg.)
Modification	3 ml. (250 mg.)	3 ml. (250 mg.)	3 ml. (250 mg.)

They state that gamma globulin should be reserved mainly for children suffering from an intercurrent illness, for those in whom an attack of measles may have a serious outcome, and for preventing an outbreak of measles in a children's ward where a case of measles has already occurred. In their view adult serum has not sufficient value in measles prophylaxis to justify the risk of serum hepatitis which its use entails.

John Lorber

793. **Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis. 5. Reanalysis of Results Based on Laboratory-confirmed Cases**

W. McD. HAMMON, L. L. CORIELL, E. H. LUDWIG, R. M. McALLISTER, A. E. GREENE, G. E. SATHER, and P. F. WEHRLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 21–27, Sept. 4, 1954. 9 refs.

In two earlier papers the authors analysed the findings of a controlled field study on the prevention of poliomyelitis by administration of gamma globulin (*J. Amer. med. Ass.*, 1952, **150**, 750 and 757; *Abstracts of World Medicine*, 1953, **13**, 339). In an average dose of 0·14 ml. per lb. (0·3 ml. per kg.) body weight gamma globulin

was found to be of doubtful value in the first week, to give highly significant protection in the next 4 weeks, and some protection for 8 weeks after injection. The diagnosis of paralytic poliomyelitis, however, was made entirely on clinical grounds. Since then, laboratory investigations have been carried out in each case, and in this paper the authors present a further analysis of their field study based exclusively on laboratory-confirmed cases. Diagnosis was judged confirmed when virus was isolated from the faeces or there was a fourfold or greater rise in neutralizing antibody in the patient's serum. The response to the complement-fixation test was accepted only when the neutralization test was not performed and there was a fourfold change in titre for only one type of virus. Poliomyelitis virus was isolated from 245 patients and contacts, 89% being of Type 1 and the remainder being almost equally distributed between Types 2 and 3. In addition, untypable and so far unidentified viruses were isolated in 16 other instances.

As a result of these laboratory examinations 9 out of 22 (41%) of the cases given gamma globulin, in which poliomyelitis was diagnosed clinically and the disease developed 4 days to 8 weeks after the injection, had to be excluded; likewise 11 out of 64 (17·2%) of the control group receiving injections of a solution of gelatin had to be excluded. This, the authors consider, suggests that types of poliomyelitis virus as yet unrecognized had produced a clinical syndrome resembling the mild or even the severe paralytic form of the disease. It is of great interest to note that of the 16 unidentified agents tested to date, none had the properties of poliomyelitis or Coxsackie virus, and that one or two of the agents produced distinct pathological changes in the spinal cord and nerve roots when injected into monkeys. The agents were unaffected by type-specific poliomyelitis antisera, a mixture of these sera, or gamma globulin. [It is to be hoped that more information on these unknown viruses, which can apparently reproduce a poliomyelitis-like clinical syndrome in man, will be forthcoming in a later communication.]

Exclusion of these unconfirmed cases from the study indicated that gamma globulin was slightly more effective against poliomyelitis than had been supposed. Protection from paralysis or modification to the extent of eliminating detectable paralysis at a muscle examination 60 days after onset probably occurred even in patients receiving gamma globulin during the week before the onset of symptoms. Protection was, however, most conspicuous during the next 4 weeks after injection, and appeared to last up to 8 weeks. Protection seemed to be by a combination of prevention and modification of the disease [as might be expected from experience of gamma globulin in the prophylaxis of measles]. The importance of these findings, in the authors' view, is that they offer very suggestive, though not conclusive, evidence of the protective value of gamma globulin after exposure and possibly, therefore, in family contacts. Further, no significant difference in the proportion of persons excreting virus was detected among contacts of the same age group between those who had received an injection of gamma globulin or gelatin solution and those who had not received an injection before exposure. This is taken to indicate that the small amount of gamma globulin given did not interfere with infection by the poliomyelitis virus. Similarly, it was shown that it did not interfere with the development of active immunity, as judged by a significant increase in neutralizing antibody titre in such contacts. *H. Stanley Banks*

794. **Studies in Human Subjects on Active Immunization against Poliomyelitis. II. A Practical Means for Inducing and Maintaining Antibody Formation**
J. E. SALK. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 994–1009, Aug., 1954. 12 figs., 4 refs.

This paper from the University of Pittsburgh is the continuation of a preliminary report (*J. Amer. med. Ass.*, 1953, **151**, 1081) on the results of inoculation of human subjects with poliomyelitis virus vaccines. The vaccines, which were prepared from all three types of poliomyelitis virus, were grown in cultures of monkey-kidney tissue and inactivated by 1:4,000 formaldehyde at 36° C.; they were non-infective but still antigenic. After inoculation the blood was examined serologically for type-specific antibody production.

In subjects who had no demonstrable antibody in the blood of the specific type, there was a response to primary inoculation within 12 days. The antibody titre, however, was the same whether the subjects had received one injection, two injections with an interval of 2 weeks between each, or 3 injections at weekly intervals. The second and third injections did not act as " booster " doses or as secondary stimuli. On the other hand, in subjects with specific natural antibody—presumably as a result of a previous infection—there was a most striking response, the antibody titre being 50 to 60 times higher than that in the first group. The antibody tended to persist in the circulation for a considerable time in the majority of the subjects in both groups, and was detectable 7 months later. A second inoculation after this interval, in the group without demonstrable antibody originally, produced a response after 12 days which was as striking as that observed in the group with previous antibody after the first inoculation. When vaccines made with different strains of the same type were used there was a closely-related immunological response.

Altogether some 4,000 children were inoculated with vaccines made in the Virus Research Laboratory of the University of Pittsburgh, and another 3,000 were inoculated with vaccines prepared at the Connaught Medical Research Laboratory, University of Toronto. With the exception of a transient urticaria in one child who was allergic to penicillin, no local or systemic ill effects were observed. (The fluid used in preparing the vaccine contained 500 units of penicillin per ml.) There were no signs of a harmful effect on the kidneys. The author states that the possibility of sensitization to the Rh factor is at present under investigation. He points out that it is still not known whether the level of antibody artificially induced by vaccines will prove sufficient to prevent the entrance of the virus to the nervous system through either blood or nerve pathways. *L. J. M. Laurent*

Industrial Medicine

795. **Emotional Aspects of Respiratory Disorders among Coal Miners**
W. D. Ross, L. H. Miller, H. H. Leet, and F. Princi. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 484–487, Oct. 2, 1954. 13 refs.

A series of 40 coal-miners aged between 36 and 64, who were referred to the Department of Industrial Health of the University of Cincinnati College of Medicine as being incapacitated by chest complaints, were subjected to numerous special medical investigations, daily observation for 3 to 6 weeks, and an interview with a psychiatrist who assumed the role of one of the group of examining physicians. None of the men had been able to work for the previous 1 to 2 years. [It is implied that they had all worked underground.]

It was found that only 5 men had no psychiatric disability, while 14 had psychiatric disability but no physical disability. The remainder had both types of disability, the physical diagnoses including pneumoconiosis, emphysema, and bronchial asthma. In cases of emphysema or bronchial asthma it was not always possible to tell whether the physical or the psychiatric disability came first, since either could have caused the other.

Thirty of the men were interviewed by the psychiatrist, who found that depressive and anxiety features predominated. Fatalities in the mines, the death of a relative, or an accident to the man himself had often been followed by an increase in symptoms. The childhood background was also examined [but unfortunately there is no record of a similar examination of a corresponding sample of normal miners; the relevance of childhood background cannot therefore be determined]. A number of psychodynamic mechanisms are postulated.

It is suggested that when a miner first complains of respiratory symptoms he should be thoroughly examined both physically and psychologically. Emotional troubles could then be treated before they caused sufficient disability to prevent him from working. An educational programme among miners concerning the psychological and physiological stresses of mining is also recommended as a preventive measure. *E. C. Poulton*

796. **Berylliosis. A Real but Preventable Industrial Disease**
H. S. Van Ordstrand. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 232–234, Sept., 1954.

This paper is based on the author's experience of 490 cases of "medical problems related to beryllium", including 98 cases of acute pneumonitis and 48 cases of chronic pulmonary berylliosis, seen at the Cleveland Clinic, Ohio. It is emphasized that the excretion of beryllium by the kidneys as indicated by its detection in the urine is proof of absorption only, not necessarily of intoxication. In chronic pulmonary berylliosis the most useful aid to diagnosis is the skin test for sensitivity, berylliosis being an allergic disease and occurring only in the hypersensitive. In the progressive type of case steroid therapy has been used by the author for the past 4 years, during which there have been no deaths in his series, whereas the mortality had formerly reached the figure of 35%.

Beryllium intoxication in industry is preventable by limiting the atmospheric concentration, the levels recommended to the United States Atomic Energy Commission by the Eisenbud Committee (1949) having proved effective. These were as follows: (1) in the plant the atmospheric concentration of beryllium should not exceed 2 μg. per c. metre throughout an 8-hour day; (2) there must never be exposure to a concentration greater than 25 μg. per c. metre; and (3) in the neighbourhood of the plant the average monthly concentration must not be greater than 0·01 μg. per c. metre. These standards can be attained by standard methods of ventilation (general and local), and it has been found in practice that the quantity of beryllium recovered from the ventilation system is sufficient to pay for the installation of the safety measures and their maintenance. The value of personal hygiene is stressed—a shower bath and a complete change of clothing before leaving the works are very necessary. *M. A. Dobbin Crawford*

797. **Degenerative Changes in the Skin with Special Reference to Jute-workers**
J. Kinnear, J. Rogers, O. A. Finn, and A. Mair. *British Journal of Dermatology* [*Brit. J. Derm.*] **66**, 344–349, Oct., 1954. 1 fig., 15 refs.

In this paper from the University of St. Andrews the authors describe the degenerative skin changes observed during a field survey of 3,023 workers in the jute industry in Great Britain. The changes included patchy pigmentation and atrophy, keratosis, telangiectasis, purpura, and occasionally carcinoma. The incidence of these changes was much higher among jute workers than among employees in other industries, including the flax industry. There was no apparent correlation between the incidence of these changes and exposure to sunlight—a correlation which has been observed in control groups—and the authors therefore consider that a specific carcinogen, presumably mineral oil, is responsible. *G. W. Csonka*

798. **Rubber-glove Eczema.** (Les eczémas aux gants de caoutchouc)
E. Sidi and M. Hincky. *Presse médicale* [*Presse méd.*] **62**, 1305–1307, Sept. 29, 1954. 8 figs., 12 refs.

The authors believe that sensitization to rubber gloves plays a significant role in the origin and development of eczema of the hands of a large number of individuals such as housewives, hairdressers, and workers in industry. In the last 5 years they have seen 102 such cases, and the incidence seems to be increasing, the number of

cases each year from 1949 to 1953 having been 6, 7, 23, 27, and 40 respectively. Gloves made of red rubber seem more prone than others to cause sensitization. In a number of cases change to an occupation in which the wearing of rubber gloves was not necessary was the only solution for the patient. *S. T. Anning*

799. **Rheumatism in the Brewing Industry.** (Rheumatismus im Brauereigewerbe)
J. Wellič. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **13**, 206–215, Aug., 1954. 5 figs., 8 refs.

Workers in the brewing industry are exposed to climatic conditions favouring the development of rheumatic diseases—frequent and violent changes of temperature, high humidity, and draughts. Of 732 such workers interviewed by the author, 142 complained of rheumatic symptoms; of these, 117 were above and 25 below the age of 32. The value of prophylaxis is stressed—provision of drying facilities for wet clothes, and access to fresh air and sunlight. The author strongly condemns the practice of providing employees with free beer as leading to flushing of the skin and thus increasing the liability to chills.

[No attempt was made to differentiate between the various types of rheumatic disorder complained of.]
D. Preiskel

800. **Experimental Administration of Ethylenediaminetetraacetic Acid in Plutonium Poisoning**
H. Foreman, P. A. Fuqua, and W. D. Norwood. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 226–231, Sept., 1954. 3 figs., 7 refs.

Of the 600 radioactive isotopes known, only about a dozen are produced in sufficient quantity and have a long enough half-life to present a serious occupational hazard. Of these the "bone-seekers" are the most dangerous—plutonium, radium, and the radioactive isotopes of strontium, barium, calcium, and some of the rare earths. Plutonium is poorly absorbed from the gastrointestinal tract, but enters the body readily by inhalation or through the raw surface of a wound and is quickly carried to the skeleton, where it will remain indefinitely, emitting a continual stream of alpha rays which may result in bone injury—osteitis, necrosis, osteogenic sarcoma—in addition to depression of the bone marrow. Apart from immediate surgical excision of the raw surface of a contaminated wound, treatment must be directed to eliminating plutonium from the body by chemical means, of which only two of those at present available show promise—the zirconium citrate procedure of Schubert and the use of ethylenediaminetetraacetic acid (EDTA). This substance forms stable, water-soluble chelates with heavy metals deposited in the bones, so that they are then rapidly excreted by the kidneys. EDTA combines readily with calcium (but more readily still with lead or with plutonium) and must be administered in the form of the calcium chelate (CaEDTA), in order to avoid depletion of the body calcium. It is ineffective in radium or strontium poisoning, since its avidity for them is less than for calcium.

The use of CaEDTA in the treatment of lead poisoning has been reported by several authors, and here 2 cases are reported of its use in the treatment of plutonium poisoning. In the first a woman laboratory technician of 40 had absorbed plutonium through a contaminated cut on her thumb. Special treatment was not started until 4 or 5 days later, when she was given 2·5 g. of CaEDTA in 250 ml. of saline by slow intravenous drip infusion twice daily for 16 days. The excretion of plutonium was markedly increased on the first day of treatment, the assay count showing a rise from 12 disintegrations per minute (d.p.m.) to 1,300 d.p.m., the quantity then gradually diminishing from day to day. It was estimated that some 20 to 25% of the original dose of plutonium was removed during the 16 days of treatment. In the second case a male chemist had been exposed to plutonium 7 years previously by inhalation of vapour spray during neutralization and oxidation of solutions containing plutonium. The amount now firmly bound in the skeleton was estimated to be about 1·2 μg. To test the efficacy of the method, on each of 5 days he was given an intravenous injection of CaEDTA in saline, the dose varying from 0·01 to 5 g., with an over-all average rise in his excretion of plutonium to 10 times the pre-treatment quantity.

CaEDTA is a relatively non-toxic drug and passes through the body unchanged unless it meets a heavy metal. Its early use is indicated in any case of poisoning by plutonium. *M. A. Dobbin Crawford*

801. **Polarographic Determination of Lead in Blood**
A. L. Nylander and C. E. Holmquist. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 183–191, Sept., 1954. 4 figs., 17 refs.

A polarographic method for the determination of small quantities of lead in blood is here described in detail. It is claimed that the method is comparatively rapid, is well suited to the routine clinical examination of workers exposed to lead hazard as it needs only 5 ml. of blood, and that it is specific for lead and of an adequate accuracy. The results are compared with those of spectrographic determination, and the possibility of interference by tin contained in the blood is discounted.

The lead is separated from the ashed blood by dissolving in dilute nitric acid and ammonium citrate solution, and, after neutralization with ammonia and addition of citrate–cyanide mixture, is extracted with a solution of dithizone in carbon tetrachloride. The lead complex is then destroyed by shaking the solution with 1N hydrochloric acid, the lead being taken up by the aqueous phase. The dithizone phase is drawn off and the aqueous phase poured into an electrolytic vessel and kept at 25° C. for at least 30 minutes while nitrogen is bubbled through to displace any dissolved oxygen. The polarogram is then recorded over the range of −0·25 to −0·7 v.

Details are given of a calibration curve prepared from samples of blood with known amounts of added lead, with statistical analysis, and values obtained by this method and by spectrography are compared.
M. A. Dobbin Crawford

Forensic Medicine and Toxicology

802. **Medical Contraindications to Imprisonment.** (Contre-indications médicales à la détention)
L. ROCHE and J. VIALLIER. *Annales de médecine légale* [*Ann. Méd. lég.*] 34, 115–118, June–July, 1954.

The authors first point out certain basic facts regarding the effects of imprisonment on the health of the prisoner and enumerate the various general and special medical facilities available under the French penal system. They then discuss the conditions in which the question of granting liberty to prisoners on medical grounds most frequently arises. (1) Pulmonary tuberculosis can rarely be treated adequately in a prison hospital, but in cases where the disease is inactive, imprisonment enables constant supervision to be exercised and prompt action to be taken in the event of a relapse. In such cases, however, the prisoner must be kept in hospital and not allowed to spread infection. (2) Cardiovascular diseases, especially hypertension and coronary thrombosis, usually constitute a contraindication to imprisonment. (3) Gastrointestinal and renal conditions requiring the enforcement of diet and temperance can frequently be treated with advantage in a prison hospital, provided psychological factors are not of primary importance. (4) Diabetes mellitus and venereal diseases can be treated adequately in prison. Prisoners developing surgical emergencies, infectious diseases, or psychoses should be transferred to appropriate non-penal institutions.

From the medical point of view, prisoners may be classified as follows: (1) those requiring treatment which cannot be satisfactorily carried out in prison, and lack of which would have grave consequences to the prisoner's health; (2) those requiring treatment not available in prison, but in whom the delay entailed by detention will not lead to deterioration in health; (3) those for whom prison life would be particularly difficult to bear owing to disabilities or disorders of behaviour, although it would not cause deterioration in their health; (4) those in whom there is no reason to suppose that imprisonment will affect health adversely; and (5) those suffering from incurable diseases with grave prognosis. It is emphasized that the judicial authority is responsible for the final decision in all cases, the physician's role being purely advisory; his recommendations should therefore be determined exclusively by the medical and humanitarian aspects of the case.

S. Karani

803. **Oral Calcium EDTA in Lead Intoxication of Children**
J. E. BRADLEY and A. M. POWELL. *Journal of Pediatrics* [*J. Pediat.*] 45, 297–301, Sept., 1954. 6 refs.

Disodium calcium ethylenediaminetetraacetate (CaEDTA) was given by mouth to 5 children at the University of Maryland School of Medicine, Baltimore, who were suffering from proved lead intoxication, all having a clinical history of eating paint or plaster containing lead. Diagnostic procedures included estimation of the lead concentration in the blood and of the urinary excretion of coproporphyrin, radiological examination of the long bones, and a haematological examination. The urinary excretion of lead was determined in 24-hour specimens by the dithizone method, with buffer extraction. The dosage of calcium EDTA was 75 mg. per kg. body weight daily, in fractionated doses at 6-hour intervals, for a period of 9 days.

The drug caused a considerable increase in urinary excretion of lead; it was well tolerated, there being no unpleasant side-effects, and anorexia and irritability disappeared. The lead content of the blood, which was increased initially, fell in all 5 patients after administration of CaEDTA. Changes in the T wave in the electrocardiogram, which were observed in 4 of the children during treatment, disappeared when the drug was withdrawn; these changes, however, could not be explained. The authors state that the amount of lead excreted in the urine is much less after oral administration of the drug than after intravenous injection, and suggest that in acute lead poisoning and in lead encephalopathy, where rapid excretion is important, the latter route is to be preferred. They conclude that CaEDTA by mouth offers some promise in the treatment of cases of chronic lead poisoning, but that the final dosage and frequency and duration of treatment remain to be determined.

P. N. Magee

804. **The Treatment of Lead Encephalopathy. A Method for the Removal of Lead during the Acute Stage**
S. P. BESSMAN, M. RUBIN, and S. LEIKIN. *Pediatrics* [*Pediatrics*] 14, 201–208, Sept., 1954. 5 figs., 14 refs.

The authors, working at the Children's Hospital, Washington, D.C., describe the results obtained with the disodium calcium salt of ethylenediaminetetraacetic acid (CaEDTA) in the treatment of acute lead encephalopathy in 7 children. In the doses employed CaEDTA was non-toxic, its use being based on its greater chelating affinity for lead than for calcium. As a result of the exchange between lead and calcium, very high levels of lead were found in the blood and urine. In spite of this the patients' condition improved, as the lead complex with CaEDTA was non-toxic and, being freely permeable, was rapidly excreted. Of the 7 patients, one who was admitted *in extremis* died after showing temporary improvement with treatment. Examination of the urine in these cases revealed that approximately 1·8 mg. of lead was excreted for each 500 mg. CaEDTA administered. The authors recommend the subcutaneous or intravenous injection of 500 mg. of CaEDTA every 8 hours for 5 days, followed by a 3-day rest period to allow for the chelating action of the drug on the lead in the bones, and then a further 5-day course.

H. B. Stoner

Radiology

805. **Irradiation of the Pituitary of the Rat with High Energy Deuterons**
C. A. TOBIAS, D. C. VAN DYKE, M. E. SIMPSON, H. O. ANGER, R. L. HUFF, and A. A. KONEFF. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 1–21, July, 1954. 18 figs., 23 refs.

The present study, undertaken at the University of California, Berkeley, was designed to demonstrate the use of deuteron radiation for the destruction of a tissue lying deep in the body. Rats were used, and the pituitary gland was chosen for study because of its well-defined volume, the ease with which it can be irradiated, and the possibility of its surgical removal so that satisfactory controls could be provided.

Approximately 1,000 rats 28 days old were used, the dosage administered varying between 3,150 and 18,900 r.e.p. The gland was completely and immediately destroyed by the highest dose, while with smaller doses it continued to increase in size for a time before undergoing atrophy, which was not complete until 9 months after irradiation. The greater the dose, the more rapid the atrophy. There was no evidence of stimulation of pituitary function, and the different types of cell in the anterior lobe were found histologically to be almost equally sensitive to irradiation. Body growth and thyroid growth were impaired soon after irradiation, but degeneration of the testes occurred much later.

Jan G. de Winter

RADIOTHERAPY

806. **Indications for Radiotherapy in Cancer of the Oesophagus. (A Statistical Study of 120 Cases.)** (Indications de la rœntgenthérapie dans le cancer de l'œsophage. (D'après une statistique de 120 cas))
J. PAPILLON and M. GOYON. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **35**, 353–364, 1954. 9 figs., bibliography.

In this paper the authors' aim is not so much to present their results in the treatment of carcinoma of the oesophagus as to define more precisely the type of case which is suitable for radiotherapy. The development of surgery and radiotherapy in this condition is outlined, and improvements in radiotherapeutic technique such as rotation and pendulum therapy are mentioned. The present place of radiotherapy in relation to surgery, palliative gastrostomy, and chemotherapy is then discussed.

A series of 120 patients with carcinoma of the oesophagus, whose average age was 55 and of whom only 3 were women, were treated by the authors at the Lyons Radiotherapy Centre between June, 1949, and June, 1952. Biopsy was performed in 74 of these cases. Irradiation was carried out through six or more beam-directed fields applied to the skin of the thorax, and a tumour dose of 5,000 to 6,000 r was given. The patients were treated lying down and a conventional 200-kV apparatus was used. The possible errors that may occur in treating a deep-seated tumour owing to the variations in anatomy, position, and respiration in the living patient are enumerated, and it is pointed out that the accurate determination of the extent of the tumour presents no less a problem. Other factors to be taken into account are the lymphatic spread from the primary tumour and the malignancy of the tumour itself, which may not necessarily be unifocal. The advanced nature of the disease in the authors' series is reflected in the fact that only 32 cases were regarded as having a favourable prognosis and classifiable as belonging to Stage I or II. The prognosis in the remaining 88 cases was regarded as poor owing to the extent and type of the tumour or the presence of lymph-node metastases, multiple primaries, cachexia, or alcoholism.

Death occurred from haemorrhage in 3 cases, and in 3 from immediate and 6 from late perforation. Mediastinitis, when it occurred, was controlled by antibiotics; 7 patients developed radiation pneumonitis. Attention is drawn to the occurrence of metastases in bone in 5 patients in this series. As a result of treatment improvement in the dysphagia occurred in more than half of the patients and radiological disappearance of the tumour in one-third. The average survival among the 32 cases in Stages I and II was 17·8 months, and among the remainder 5·6 months, giving an over-all average survival of 8·8 months. Three patients survived more than 2 years.

It is concluded that radiotherapy is indicated in cases of moderately extensive carcinoma of the oesophagus without evidence of metastasis. Such treatment, carried out with careful attention to technique, will at least relieve dysphagia and, in favourable cases, may result in cure.

R. D. S. Rhys-Lewis

807. **Telangiectasis as a Late Effect of *X*-irradiation.** (Die Röntgentelangiektasie als Spätsymptom)
G. MIESCHER, J. PLÜSS, and B. WEDER. *Strahlentherapie* [*Strahlentherapie*] **94**, 223–233, 1954. 10 figs., 11 refs.

At the University Dermatological Clinic, Zürich, the authors have observed for a minimum period of 5 years a number [unstated] of cases of malignant tumour which had been treated by irradiation with a view to determining the relation between radiation dose, quality of beam, and size of field on the one hand, and the development of telangiectasia and its time of onset and extent on the other. It was found that for a given dose the number of cases developing telangiectasia increased with the years, that the reaction developed its maximum intensity only after at least 5 years, and that the strength and

penetration of the beam were of no significance. They also noted that the skin of the face appeared to be less predisposed to develop severe telangiectasia than that of the trunk or extremities, and for this reason they recommend the use of repeated small doses of irradiation in preference to a large single dose for the treatment of extensive lesions of the trunk or extremities if a good cosmetic result is to be obtained. *Jan G. de Winter*

808. **Radioactive Iodine in Malignant Melanoma**
R. C. KORY, R. G. TUCKER, and G. R. MENEELY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 119–123, July, 1954. 8 refs.

The present study was undertaken at Thayer Veterans Administration Hospital and the Vanderbilt University School of Medicine, Nashville, Tennessee, to explore the possible usefulness of radioactive iodine (^{131}I) as a therapeutic agent in malignant melanoma—tyrosine being metabolized by the epidermal melanoblast to form melanin, it was hoped to incorporate the ^{131}I in the melanomatous tissue in this way. Eight patients with malignant melanoma were given oral doses of 50 to 65 mc. of ^{131}I as sodium iodide. In none was there any evidence of selective uptake of ^{131}I, nor could any discernible alteration in the course of the disease be demonstrated. *Jan G. de Winter*

809. **Treatment of Polycythaemia Rubra Vera with Radioactive Phosphorus**
D. VEREL. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 857–859, Oct., 1954. 2 figs.

Polycythaemia rubra vera has been treated with radioactive phosphorus (^{32}P) at the London Hospital for the past 3½ years. The results in 18 cases treated so far are discussed, 3 cases of varying severity being described in detail. They show that the erythrocyte count and haematocrit reading give an accurate assessment of the effect of ^{32}P only when the total blood volume is normal (although the author does not consider that blood volume measurements are a necessary part of the therapeutic control of the disease). In all his cases, when the venous haematocrit value was reduced to normal by treatment, then the blood volume also became normal. When a fall in the number of erythrocytes and in the haematocrit reading was unassociated with a reduction in blood volume the symptoms were usually unchanged, whereas a marked fall in volume even with little change in the erythrocyte count often produced dramatic symptomatic improvement. The usual blood findings in the disease are represented in schematic form.

Assessment of the value of treatment was related to the duration of remission. The tabulated results in 11 cases not previously treated indicate that doses of ^{32}P giving 3 to 7 mc. resulted in remissions of 3 to 27 months. In 8 cases previously treated by deep *x*-ray therapy and then given 3 to 7 mc. of ^{32}P remissions ranged from 4 to 30 months. The clinical response and changes in the blood are also tabulated. The author cites the case of one patient who was treated for 4 years only by venesection, a total of 25 pints (14 litres) of blood being removed. This patient did not respond to 7 mc. of ^{32}P and it is suggested that the bone marrow hyperplasia which continued in the absence of treatment would account for the need for higher dosage. In 5 of the cases the increasing duration of remissions after repeated treatment with ^{32}P is attributed to either the disease dying out or its slow cure; the author favours the latter view. *G. E. Flatman*

810. **Some Experiences with Radioactive Phosphorus in the Treatment of Mycosis Fungoides**
F. E. NEAL. *Proceedings of the Royal Society of Medicine* [*Proc. roy, Soc. Med.*] **47**, 859–864, Oct., 1954. 6 figs., 3 refs.

At the Sheffield National Centre for Radiotherapy 5 cases of mycosis fungoides were given prolonged treatment with multiple injections of radioactive phosphorus (^{32}P). The author points out that there is increased uptake of ^{32}P in tissues exhibiting high metabolic activity, as do these skin lesions. The dosage of ^{32}P, which was empirical and was controlled by the blood picture and the general condition, ranged from 8 mc. in 6 weeks to 39 mc. in 23 weeks, the injections being given at approximately monthly intervals and biopsy specimens taken from the lesions and compared with normal skin during the ensuing 14 days. The doses calculated are tabulated and the greater uptake in the lesion than in the blood and skin expressed graphically. The uptake in blood and bone marrow was comparable to that in normal skin and was relatively low, but even so the patient given 39 mc. developed marked thrombocytopenia; a slower dosage rate is suggested to avoid this. In the other 4 cases the blood picture remained within normal limits throughout.

Of the 2 patients with premycosic erythrodermia, one improved rapidly and was free of symptoms and signs one year later, but the other had only slight relief from pruritis. Of the 3 patients with widespread mycotic lesions, one obtained temporary relief from pruritis, the lesions on the face of the second improved though subsequently others developed elsewhere, but the third, after 4 months' improvement in the lesions on the trunk and limbs, relapsed and later died from intercurrent infection. Since the aim of this treatment was mainly palliative the author considers that the relief from pruritis in 4 of the cases was a worth-while result. In his view *x*-ray therapy remains the treatment of choice for localized lesions of this disease. *G. E. Flatman*

811. **The Distribution and Radiation Effects of Intravenously Administered Colloidal Au^{198} in Man**
S. W. ROOT, G. A. ANDREWS, R. M. KNISELEY, and M. P. TYOR. *Cancer* [*Cancer (N.Y.)*] 7, 856–866, Sept., 1954. 7 figs., 13 refs.

A preliminary investigation is reported from the Oak Ridge Institute for Nuclear Studies, Oak Ridge, Tennessee, of the immediate effects of intravenous injection of colloidal radioactive gold (^{198}Au) in human beings, and of its use in the treatment of neoplasms in the liver. The 7 cases here described were terminal ones and no physical improvement was noted. The doses of ^{198}Au

given in these 7 cases were respectively 2·3 mc., 10 mc., 20 mc. spread over 6 weeks, 33 mc., 60 mc. spread over 4 weeks, 63 mc. in 5 days, and 105 mc. in one injection. The concentration of ^{198}Au in the blood and tissues was measured by Geiger counter, and in tissue obtained post mortem the dry weight of gold was assessed. Autoradiographs were taken of bone and various organs. It was found that most of the gold given intravenously had left the circulation by the time the injection was completed (10 to 30 minutes). As was expected, the greater part of it was taken up by the liver, but autoradiographs showed that it was concentrated in normal liver tissue, the liver metastases containing little or no gold. This applied also to the spleen and bone marrow.

The authors conclude that intravenous administration of colloidal ^{198}Au is of no promise in the treatment of discrete primary or metastatic lesions of the liver, but the possibility of treating very fine diffuse lesions in this way is not entirely ruled out. *E. Stanley Lee*

812. **Treatment of Prostatic Carcinoma with Radioactive Colloidal Chromic Phosphate (P^{32}): a Preliminary Report**

C. RUSCHE and H. L. JAFFE. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 466–475, Sept., 1954. 5 figs., 12 refs.

The purpose of this report is to evaluate the results of the treatment of 28 patients with carcinoma of the prostate by the injection of radioactive colloidal chromic phosphate (^{32}P) over a period of one year at the Cedars of Lebanon Hospital (University of Southern California School of Medicine), Los Angeles. This form of treatment was started because certain features of the treatment by injection of radioactive colloidal gold (^{198}Au) were considered to be unsatisfactory, its short half-life being inconvenient when transport over long distances is necessary, and the emission of gamma rays adding a health hazard to personnel without (in the authors' opinion) therapeutic advantage and possibly causing bone-marrow depression. Radioactive colloidal chromic phosphate was chosen as an alternative since it can be made in the laboratory from the soluble form of ^{32}P, has a convenient half-life of 14·3 days, and is a pure beta-ray emitter, this simplifying the protection precautions necessary. It was found that 1·5% of the injected material was excreted in the urine in 24 hours and only an additional 1% in the next 6 days. It was therefore concluded that 97·5% of the material stayed at the site of injection. Injection was made both perineally and transvesically, the primary tumour and all palpable lymph nodes being infiltrated. Multiple needles were inserted into the substance of the prostate and from 0·3 to 0·5 mc. injected for each gramme of tissue, the largest amount injected in any single case in the series being 40 mc. The solutions used contained from 1 to 3 mc. of chromic phosphate per ml. and also hyaluronidase and adrenaline in an attempt to increase local spread and diminish the risk of absorption into the blood stream.

There was no change in the size of the prostate in 10 of the 28 cases and a decrease in 18, in 14 of which the change was "remarkable". The changes found in samples removed for biopsy at intervals after treatment were not so striking as was expected from the clinical response. Radioactivity was detected in this tissue up to 3 months. In one patient 12 months after treatment there was extensive fibrosis throughout the areas taken for section, with tumour cells showing signs of radiation damage. In no case was it possible to show that the tumour had been eradicated, but the local reactions seen suggested that if thorough dispersion of the isotope through the involved tissue could be obtained, destruction of the cancer should result. No serious complications were encountered, but some bowel irritation with oedema of the rectal wall was seen. Mild bladder symptoms occurred in nearly all cases.

D. Waldron Smithers

813. **Intraprostatic Injections of Radioactive Colloids. II. Distribution within the Prostate and Tissue Changes following Injection in the Dog**

G. J. BULKLEY, J. A. COOPER, and V. J. O'CONOR. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 476–484, Sept., 1954. 6 figs., 4 refs.

Experiments were carried out at Northwestern University Medical School, Chicago, in an attempt to determine the local effect, and that on distant organs, of the injection of radioactive colloids into the prostate of the dog. Ten experiments were carried out with radioactive colloidal chromic phosphate (^{32}P) and 9 with radioactive colloidal gold (^{198}Au), the animals being killed at intervals of 2 weeks to 3 months after the injection in the former case and of 1 to 7 weeks in the latter. No appreciable radiation effect was noted in organs distant from the prostate, with the sole exception of the regional lymphatics following an injection of radioactive gold. Distribution of the colloidal material throughout the prostate was not uniform in any instance, and in none of the animals was destruction of the normal prostate complete. Periprostatic reaction was more marked after the injection of radioactive gold than of the phosphate.

D. Waldron Smithers

RADIODIAGNOSIS

814. **The Diencephalic and Endocrine Reaction to Air Encephalography.** (La réaction diencéphalo-endocrinienne de l'encéphalographie gazeuse)

G. BOUDIN, J. BARBIZET, and J. LEPRAT. *Presse médicale* [*Presse méd.*] **62**, 1243–1245, Sept. 22, 1954. 3 figs., 19 refs.

It has previously been shown by various workers that the introduction of air into the subarachnoid space produces definite effects upon the hypophysial and diencephalic regions, leading to subsequent modifications in endocrine and other functions. The present study deals with the variations so produced [but does so in a somewhat patchy fashion, mingling references to earlier work with recent observations in a rather confusing manner].

It appears, however, that among the changes caused may be the following. (1) An antidiuretic effect of an unstated duration, which the authors attribute to the hypersecretion of antidiuretic hormone. (2) Moderate

elevation of the body temperature within a period of 5 days of the investigation, noted in 16 out of 26 of the authors' cases and attributed to disturbance of the thermo-regulating centre. (3) Sleep disturbance has been reported, but is rejected in view of the complications introduced by morphine therapy. (4) Changes in the blood picture, consisting in initial lymphocytosis followed by lymphopenia, maximal at 4 hours, and by eosinopenia; a comparable fall in the number of eosinophils was not noted after simple lumbar puncture. (5) A temporary hyperglycaemia, reaching a maximum after 30 minutes [no original observations were made by the authors on this]. (6) Thyroid reactions. Comparative fixation tests of radioactive iodine by the thyroid gland at 6 and 24 hours after an initial dose of ^{131}I, both before and again 72 hours after pneumoencephalography in 10 cases [no controls seem to have been used] showed an increased fixation level following the performance of encephalography. Again the mechanism of action is considered to be via the diencephalon and hypophysis. (7) Brief allusion is made to the possible effect upon genital function, but little work has been done in this field.

The probable mechanism of production of these effects is discussed, and it is suggested that the hypothalamic region plays its part in producing these changes through the hypophysis. The authors conclude with the suggestion that pneumoencephalography might be used to test diencephalic–hypophysial function, and the results, in conjunction with observations of the effects of ACTH and thyroid stimulating hormone, might lead to the identification of the level of the defect in endocrine disorder by establishing the differences between a central diencephalic, a pituitary, or a peripheral glandular failure.

L. A. Liversedge

815. Complications of Cerebral Angiography

A. D. KAPLAN and A. E. WALKER. *Neurology* [*Neurology*] **4**, 643–656, Sept., 1954. 1 fig., bibliography.

A detailed review is presented of the complications occurring during the performance of cerebral angiography on 500 consecutive occasions at the Johns Hopkins Hospital, Baltimore, between February, 1951, and April, 1953. There were 484 patients, of whom 248 were males and 236 females; local analgesia was used for all patients of 12 years and over, except for 15 who were uncooperative. Direct puncture of the carotid artery was made on 491 occasions and of the vertebral artery on 8, and there was one open operation (on a child). The medium used was 35% diodone, the total dose being 30 to 90 ml. for adults and 10 to 30 ml. for children under 12, given in injections of 10 to 15 ml. and 5 to 8 ml. respectively. Lateral and antero-posterior stereoscopic views were taken in the majority of cases to show the arterial, capillary, and venous phases, 12 films being exposed.

In the whole series of 500, non-fatal complications occurred in 19 patients, and 17 others died before leaving hospital; 13 of these deaths were considered not to be due to angiography, however, so that the mortality was 0·8% and the total incidence of complications, fatal and non-fatal, was 4·6%. Motor or sensory disturbances occurred in 10 cases, and in all but one they cleared up within 48 hours. Convulsions occurred in 3 cases, but 2 of the patients affected were known to be subject to seizures. Visual disturbances are not uncommon after cerebral angiography, but in most cases are temporary; of the 2 patients so affected in this series, one developed a large right central scotoma lasting 48 hours, and the other bilateral blindness lasting 4 days, visual acuity being normal a month later, although visual agnosia persisted. General or systemic complications included mild fever lasting for one to 3 days, and urticaria in 2 cases, while a local haematoma developed in 2 others.

Death following cerebral angiography in cases of cerebral tumour is thought to be due to cerebral oedema caused by diodone, with resultant herniation of the brain through the tentorium or foramen magnum, while additional thromboses and haemorrhages may occur in cases of cerebral vascular disease. Race and sex do not appear to influence the incidence of complications, but they tend to occur more often among patients over the age of 50, while those with vascular disease are more frequently affected than those with neoplastic or convulsive disorders. A decrease in the rate of the cerebral circulation appears to increase the liability to complications. The mechanisms producing complications have been the subject of extensive investigations which have not so far produced any definite conclusion, but vasospasm, increased capillary permeability, irritation of neurones, embolism, allergy, and the technique of arterial puncture are among the factors considered to be of importance.

W. B. D. Maile

816. The Diagnosis of Cardiac Shunts by Intravenous Angiocardiography

J. LIND, R. SPENCER, and C. WEGELIUS. *British Heart Journal* [*Brit. Heart J.*] **16**, 407–416, Oct., 1954. 9 figs.

Angiocardiography, particularly when used in conjunction with electrocardiography, can give valuable information about the internal dynamics of the heart and is particularly valuable in the diagnosis of congenital shunts, when the cardiac silhouette as visualized in conventional radiographs may differ little from the normal. The angiocardiograms here presented from the Karolinska Institute and the Wenner-Gren Cardiovascular Research Laboratory, Stockholm, were all taken simultaneously in the right and left oblique projection at the rate of 10 to 12 per second. The patients were infants or young children and the contrast medium (70% "umbradil") was injected into the malleolar or antecubital vein in a dose of 1 to 1·5 ml. per kg. body weight.

Right-to-left shunts are usually well shown since the left side of the heart is free of medium at the outset. It is important, however, that one of the views should show the plane of the interatrial septum end-on; success or failure to see the shunt may also depend upon the phase of contraction of the atrium at the moment of arrival of the medium. Although a right-to-left interatrial shunt is generally easy to recognize, the authors discuss the case in which an apparent shunt seen during diastole may be due to the presence of a patent foramen

ovale or a true septal defect, so that with too great a pressure of injection the usual direction of such a shunt may be momentarily reversed. Interventricular shunts are not usually identified as jets of opaque medium owing to dilution of the medium by residual blood in the ventricle; in such cases diffuse opacification of the left ventricle occurring within the first two or three cardiac cycles is then the main criterion of a shunt. In cases of a high septal defect, or where the aorta overrides, the latter may be filled even before opacification of the left ventricle. When a patent ductus arteriosus is accompanied by a right-to-left shunt, early filling of the descending aorta is the main feature.

The diagnosis of left-to-right shunts depends upon an understanding of the rate of dilution of the contrast medium in the successive chambers of the normal heart. Persistence of an abnormal degree of opacification in the right atrium is suggestive of an interatrial defect with a left-to-right shunt; this is usually accompanied by enlargement of the right atrium. When an interventricular shunt is from left to right, rapid dilution of the opaque medium by blood from the left side during systole may be discerned. There is also, as in the atrial defect, prolonged opacification of this chamber, as well as of the pulmonary artery, and the left atrium is usually dilated. The presence of a patent ductus arteriosus with a left-to-right shunt may be suggested by a rapid loss of contrast in the pulmonary artery, owing to the influx of blood. Other diagnostic evidence may be obtained by a careful study of different phases of the cardiac cycle, as the moment when the contrast medium reaches the heart will influence the degree of opacification in the aorta, right ventricle, and pulmonary artery.

[Unfortunately some of the angiocardiograms reproduced suffer from too great reduction, and do not adequately bring out the authors' points.]

A. M. Rackow

817. **Portal Venography in Banti's Disease**
G. H. Du Boulay and B. Green. *British Journal of Radiology* [*Brit. J. Radiol.*] 27, 423–434, Aug., 1954. 22 figs., bibliography.

Believing that the indications for operation in portal hypertension are clinical, the authors contend that venography at laparotomy is preferable to splenic-puncture venography (with its risk of splenic rupture or severe bleeding) and that it provides the surgeon with just as much information on which to base his choice of operation. Their method is as follows. A double cassette tunnel incorporating a grid is used, enabling one exposure to be made immediately at the end of injection of 30 ml. of 70% diodone (15 ml. in children) and a second exposure about 1·75 seconds later. Fast film and high-kV screens are used, with an exposure of 0·6 to 0·8 second at 80 to 85 kV and 40 to 45 mA, the anode–film distance being 36 inches (0·9 metre). The contrast medium is usually injected into a jejunal vein or into the spleen, and the films taken in antero-posterior projection. The results of examination of 46 patients in this way at St. Bartholomew's Hospital, London, are here reported. It is pointed out that hypertension may be due to intrahepatic block in cirrhosis, or the obstruction may be extrahepatic owing either to replacement of the portal vein by scar tissue or its transformation into a cavernomatous mass. Scarring may be secondary to thrombosis from various causes or may be the result of an extension of the obliterative process in the umbilical vein and ductus venosus at birth. In 37 of the cases examined the portal vein was shown to be suitable for portacaval anastomosis, while in the other 9 a cavernomatous formation replaced the portal vein. Thrombosis causing narrowing of the lumen was shown in 3 cases, but this should not be confused with the occasional tendency for diodone to run along one side of the portal vein. In 5 cases a venogram was obtained at a second operation, an anastomosis having been previously performed; in none of these could any flow through the anastomosis be demonstrated.

Study of the vessels in the cirrhotic liver showed that the finer vessels run an irregular course and the finest branches arise earlier in the arborization than normal. From the two radiographs taken at a short interval a rough indication of the degree of stasis may be obtained. The authors suggest that the method described is of value in indicating which veins are available and suitable for anastomosis, and was useful in one case in demonstrating the presence of unsuspected gastric varices.

Kenneth A. Rowley

818. **Intravenous Cholecystography and Cholangiography: Clinical Trials with a New Medium (Biligrafin)**
D. Sutton and J. V. Tillett. *British Journal of Radiology* [*Brit. J. Radiol.*] 27, 575–581, Oct., 1954. 7 figs., 10 refs.

The authors report their experience of intravenous cholecystography using "biligrafin", the sodium salt of N:N′-adipic-di-(3-amino-2:4:6-triiodobenzoic acid). The method has the great advantage of eliminating the factor of variable absorption which is inherent in contrast media taken by mouth. Biligrafin was found to be rapidly excreted in the bile in a concentration sufficient to be detected radiographically; there was no appreciable reabsorption from the bowel. Normally only about 10% of the medium is excreted by the kidneys, but in the presence of liver damage the proportion excreted by this route may be increased. The technique employed by the authors at St. Mary's Hospital, London, was as follows: 20 ml. of a 20% solution of biligrafin was injected slowly intravenously during a period of 4 minutes, the patient having fasted overnight. Routine radiographs were taken in the prone left anterior oblique position at 15 and 30 minutes to show the bile ducts, and at 2 hours to show the gall-bladder, a large cone being used at first, but once the ducts had been visualized a small cone was used. Additional films were taken if indicated.

A total of 120 consecutive patients referred for routine cholecystography were examined by this technique, and the results are compared with those in a series of 100 patients given "telepaque" by mouth. In the biligrafin series the gall-bladder was visualized in 92% of cases, the common bile-duct in 98%, and the hepatic ducts in

83%; the corresponding figures when telepaque was used being 90%, 11%, and 0%. The gall-bladder shadow tended to be less dense with biligrafin than with telepaque, but was adequate for diagnosis. Visualization of the bile ducts in the absence of gall-bladder filling occurred only with biligrafin and this proved particularly valuable in revealing the site of the lesion—for example, a stone in the cystic or common bile duct.

The toxic effects of telepaque were not investigated in this study, but an incidence of nausea, vomiting, and diarrhoea in from 20 to 40% of cases has been reported in the literature. The toxic effects due to biligrafin noted in the present series were as follows: nausea 12 cases, retching 3, vomiting one, flushing of the skin 4, repeated sneezing one, and bouts of coughing one. In one case there was a peculiar reaction 10 minutes after the injection of the biligrafin, the patient having momentary loss of consciousness, pallor, and a faint pulse, but this reaction was not so severe as that described by Ward (*Lancet*, 1954, **1**, 887). The authors conclude that the incidence of toxic effects is much lower with biligrafin than with telepaque.

Biligrafin was also given to 10 patients with present or recent evidence of jaundice. Apart from vomiting in one case there were no toxic reactions. No satisfactory visualization of the biliary tract, however, was obtained in these cases. *G. Ansell*

819. **Operative Cholangiography**
E. S. R. Hughes and R. H. Kernutt. *British Medical Journal* [*Brit. med. J.*] 2, 620–623, Sept. 11, 1954. 2 figs., 13 refs.

Operative cholangiography was performed at the Royal Melbourne Hospital on 50 patients undergoing surgical treatment for gall-stones. After the abdomen was opened and just before the biliary tract was dissected, diodone solution was injected into the common bile duct and radiographs were taken. In 32 cases the cholangiogram appeared normal; in 12 stones were seen as filling defects; in 3 no diodone entered the duodenum, and in 2 of these stones were found; and in 3 the cholangiogram was considered to be abnormal, but no stones were found. In 10 of the 14 cases in which gall-stones were found diodone was injected after the duct had been explored, but before the abdomen was closed (control operative cholangiography). In one of these a stone was found which had been overlooked. The authors consider that control operative cholangiography is much more useful than postoperative cholangiography.
G. A. Smart

820. **The Radiological Diagnosis of Lower Urinary Obstruction in the Early Years**
D. I. Williams. *British Journal of Radiology* [*Brit. J. Radiol.*] 27, 473–483, Sept., 1954. 10 figs., 2 refs.

To determine the actual site and the exact nature of lesions causing chronic urinary obstruction in infants and children radiological examination is necessary, there being a much greater variety of such lesions in children than in adults. The present author describes the radiological methods employed and the types of obstruction observed in patients at the Hospital for Sick Children and St. Peter's and St. Paul's Hospital, London. It is pointed out that intravenous pyelography should not be attempted in a child with a blood urea level exceeding 100 mg. per 100 ml. In most cases intravenous pyelography reveals the effects of the obstruction but seldom its nature, although in mild cases radiographs of the bladder taken before, during, and after micturition may suffice. In other cases the simple urethrogram rarely assists, and it is necessary to fill the bladder through a catheter with 10 to 15% diodone (sodium iodide should not be used). Antero-posterior, lateral, and oblique views are advised in the various phases. This method presents some difficulties in young children; it is impracticable in infants, and is contraindicated if the obstruction is at all severe and renal function is depressed, in view of the risks of infection with unrelieved obstruction. In these cases the author recommends that a cysto-urethrogram should be taken on the operating table, with manual pressure to expel the opaque medium into the urethra. This is only possible in infants, and in older children with a nerve lesion of the bladder.

Obstruction in the anterior urethra is rare, but in the posterior urethra of the male obstructing valvular folds of mucosa are relatively common and are difficult to identify on urethroscopy. The posterior urethra, dilated down to the perineal membrane, is bulging and elongated. In some unusual cases with an obstruction at a similar level the urethra may be tapered, not bulging. The nature of this lesion is uncertain; a somewhat similar picture may be observed in agenesis of the abdominal musculature. In neurological disorders urethral dilatation is observed more frequently in girls than in boys, and extends down to the external sphincter; when dilatation is present in boys it extends only as far as the verumontanum.

Radiological evidence of bladder-neck obstruction is difficult to obtain. In lateral radiographs a forward projection of the posterior lip of the neck of the bladder is characteristic. Obstruction is occasionally associated with a ureterocele-like dilatation of the termination of an ectopic ureter just below the bladder neck. The shape and size of the bladder are of little importance in the diagnosis of obstructive lesions.

Uretero-vesical reflux is common, but its significance is difficult to assess radiologically. Ureteric dilatation is much more marked in infants than in adults, and may be markedly asymmetrical even with obstruction to the bladder outlet. *Kenneth A. Rowley*

821. **The *X*-ray Diagnosis of Coeliac Disease**
R. Astley and J. W. Gerrard. *British Journal of Radiology* [*Brit. J. Radiol.*] 27, 484–490, Sept., 1954. 6 figs., 9 refs.

It has already been shown that the so-called "deficiency pattern" in the small bowel can be induced in healthy subjects by administration of a variety of substances in addition to a simple aqueous suspension of barium sulphate, and that alimentary mucus has a powerful clumping effect on simple suspensions. In steatorrhoea mucus-resistant preparations reveal dilatation of the small intestine.

At the Children's Hospital, Birmingham, radiographs were taken after administration of a simple aqueous suspension of barium sulphate to 37 healthy children and 30 children with coeliac disease, and again after administration of a commercial mucus-resistant preparation to the group with coeliac disease. The findings with the simple suspension were classified according to the degree of clumping, and those with the mucus-resistant preparation according to the degree of dilatation. All degrees of coeliac disease were represented.

The investigation confirmed that in children under the age of 14 years even gross clumping had little significance. With the mucus-resistant preparation a reasonably high proportion of definite abnormalities was noted. An additional examination with the simple preparation did not provide any further help. Comparison of the clinical, biochemical, and radiological findings showed that there was a rough, but not precise, correlation between the severity of residual abnormality in late coeliac disease and the degree of dilatation of the small intestine.

The authors consider that with a mucus-resistant preparation dilatation can be detected in a significant proportion of patients with coeliac disease, including borderline cases and patients in the later stages of the disease, and that in the borderline case this may help to confirm the diagnosis. *Kenneth A. Rowley*

822. **A Roentgen Study of Osteogenic Sarcoma Developing in Paget's Disease**
R. S. SHERMAN and K. Y. SOONG. *Radiology* [*Radiology*] **63**, 48–58, July, 1954. 12 figs., 19 refs.

In order to collect information which might help in the early detection of sarcoma supervening on Paget's disease, the authors have analysed the clinical and radiological features of 19 such cases seen at the Memorial Center, New York, in all of which the diagnosis had been confirmed by biopsy.

The average age of the patients was 60; the eldest was 75 years of age, only 3 being under 50. The sex ratio, 2 males to one female, was about the same as that observed in cases of uncomplicated osteogenic sarcoma. The tumour type varied, 14 being purely lytic, 7 mixed, while one was sclerotic. In 15 patients there was a single focus of malignant disease, while in 3 there were two cancerous areas. In a further case a single sarcoma accompanied two osteolytic lesions in normal bone; these were assumed to be metastases.

The patients complained of pain, "arthritis", or the presence of a swelling. In 3 cases fracture at the site was the presenting feature. In 11 cases symptoms had been present for more than a year. The 22 sarcomata were found in the following bones: humerus, 8; pelvis 5 (ischium 2, ilium 2, pubis 1); skull, 4 (cranial vault 3, mastoid 1); femur, 2; scapula, 1; tibia, 1; and radius, 1. Attention is drawn particularly to the 3 cases in which sarcoma occurred in the cranial vault, since osteogenic sarcoma at this site is rare. In each case the tumour presented as a pulsating mass.

Radiologically the lesions appeared osteolytic with fairly well circumscribed boundaries. Periosteal reaction was a rare finding, and in no case was typical radial spiculation seen. Only 3 of the tumours invaded a joint; none had crossed into contiguous bones. *X*-ray therapy was given to 12 patients, only one of whom survived 5 years. Pulmonary metastases occurred in 11 cases.

The authors emphasize the frequency of osteolytic tumours, and suggest that the rapid growth of the tumour, the absence of periosteal reactions, and the presence of pulsation in the swelling may help to suggest the diagnosis. *A. M. Rackow*

823. **Retrograde Pyelography with Hydrogen Peroxide in the Contrast Medium: a Preliminary Report.** [In English]
P. KLAMI. *Acta radiologica* [*Acta radiol. (Stockh.)*] **42**, 181–188, Sept., 1954. 5 figs., 5 refs.

In order to improve the demonstration of ulcerative processes in the renal pelvis and calices, the author, at University Hospital, Uppsala, tried the addition of hydrogen peroxide to the contrast medium used in retrograde pyelography. The medium was prepared by adding saline and 30% hydrogen peroxide to "uriodone" (diodone) to make a solution containing 35% diodone and 1·5 or 3% of hydrogen peroxide. When only a few erythrocytes and leucocytes were noted in the specimen of urine the hydrogen peroxide content of the medium was 3%, but when these cells were present in large numbers the hydrogen peroxide content was 1·5%.

Foam, which formed at the site of the ulceration, removed the contrast medium and filling defects were more clearly seen. The author describes 4 cases in which this method was used, and gives details of the radiographic technique employed. *W. B. D. Maile*

824. **Lead EDTA Complex. A Water-soluble Contrast Medium**
N. SAPEIKA. *South African Medical Journal* [*S. Afr. med. J.*] **28**, 759–762, Sept. 4, 1954. 4 figs., 13 refs.

Lead in combination with ethylenediaminetetraacetic acid (EDTA) forms a stable, soluble, non-toxic compound which is rapidly excreted from the body. At the University of Cape Town the author has studied the possibility of using lead EDTA as a contrast medium. There is as yet no evidence that this complex is metabolized or absorbed by the body, and since all the author's experiments were carried out on animals its effects on the human body are unknown. It can be given by mouth, subcutaneously, or intravenously, and the concentration can be varied by dilution with water. In the animal experiments good visualization of the gastrointestinal, renal, and vascular systems was obtained.

[While lead EDTA seems to have many advantages over the contrast media at present in use, further work is required to determine the largest effective dose that can be given by injection and the possible toxic manifestations in human beings.] *N. Kaplan*

825. **The Value of the Routine Chest *X*-ray Film in Detecting Diaphragmatic Hernia. A Report of 53 Cases**
A. FROMAN. *Diseases of the Chest* [*Dis. Chest.*] **26**, 457–463, Oct., 1954. 5 figs., 4 refs.

History of Medicine

826. **"English Sweat"**
G. H. SMYTH. *Medical World* [*Med. Wld* (*Lond.*)] **81**, 299–303, Sept., 1954.

In 1485 a disease of great virulence appeared in England for the first time and came to be known as "the sweating sickness". Some half-dozen major epidemics occurred up to 1551, after which the disease disappeared and it has never been reliably identified. The author of this brief paper glances at some of the features of the disease and discusses once again the problem of its essential nature. The disease was dramatically sudden in onset and in fatal cases death occurred within 36 hours, sometimes within 3 hours. The continent of Europe, Scotland, and Ireland were relatively unaffected, though northern Europe suffered in the later epidemics. One of the leading physicians of the day, Dr. Caius, who gave his name to the Cambridge college, described the symptoms fully. He stated that the first manifestation was a sense of apprehension, which was followed by shivering, vomiting, severe pains in the head, neck, and limbs, thirst, delirium, and coma. Contemporary descriptions suggest that it was an infection with severe intracranial effects. There is no evidence that it left any permanent disability.

[This article is much over-simplified and should be read with caution.] *Calvin P. B. Wells*

827. **Marcello Malpighi (1628–1694).** [In English]
G. BARBENSI. *Scientia medica Italica* [*Sci. med. ital.*] **3**, 3–13, July–Sept., 1954.

Marcello Malpighi, the son of a well-to-do farmer, was born at Crevalcuore, near Bologna, on March 10, 1628. At the age of 17 he went to Bologna to study philosophy under Natali, but following the death of his parents and on Natali's advice he turned to medicine. His principal teachers, the anatomist Bartolomeo Massari (whose daughter he married in 1653) and the physician Andrea Mariani, were leaders in the struggle that was being carried on at that time against authoritarianism in medicine, especially as represented by Galenism and the Arabian school. In 1651 he received his degree in philosophy and medicine; in 1656 he was appointed Public Lector in the medical faculty of Bologna. Almost immediately, however, he was invited to the University of Pisa, where a chair of theoretical medicine had been specially founded for him by the Grand Duke of Tuscany. Here he became the friend and disciple of Giovanni Alfonso Borelli, whose influence, added to that of his former teachers, confirmed his adherence to the method of observation and experiment.

Many of his most famous discoveries originated at Pisa, but the climate was not congenial to his health and after three years he returned to Bologna. Here he began to publish the results of his researches and, although he encountered violent opposition, his fame spread far and wide. In 1662 he was called to the chair of medicine at Messina, but in 1665 he returned once more to Bologna. After 1671 he retired from practice and devoted himself to scientific research. Even now his opponents did everything possible to belittle his achievements and, not content with deriding him in anonymous pamphlets, they even assaulted him in his own home. His last years were spent at Rome under the patronage of Pope Innocent XII, whom he had earlier treated at Bologna and whose "protomedico" he now became. In July, 1694, he had a cerebral haemorrhage which resulted in hemiplegia, and he succumbed to a second attack four months later.

Malpighi was one of the first biologists to cultivate the vast field of research which had been opened up by the invention of the microscope. His greatest achievements were in human, comparative, and plant anatomy. First in his great series of researches was that on the structure and function of the lungs. He forged the final link in the chain of evidence required to complete the demonstration of the circulation of the blood by his discovery of the capillaries in the lung and in the mesentery of the frog (1661). This was followed by painstaking research on the spleen, kidney, liver, brain, and tongue, all of which led to new and exact descriptions of structure and function and which are to this day commemorated in anatomical nomenclature. His histological studies extended to every part of the animal and vegetable kingdoms. He was the real founder of plant embryology, and he also made important contributions to animal embryology in his works *De ovo incubato* and *De formatione pulli in ovo*. During his stay in Messina he began a regular correspondence with the Royal Society in London, and in 1669 he was elected an Honorary Member of that body. The Royal Society sponsored the publication of many of his most important writings, including his famous work on the silkworm (1669), his *Anatomia plantarum* (1675–9), and his *Opera posthuma* (1697). Malpighi was a tireless investigator, an exact observer, and a fearless advocate of the truth. He was also endowed with a high capacity for generalization and induction. During his lifetime and in his own country he had to contend with bitter adversaries who were blind to every argument and form of demonstration, but his position as one of the greatest medical scientists has long been secure. *W. J. Bishop*

828. **Medicine and Natural History in the Itinerary of Rabbi Benjamin of Tuleda (1100–1177)**
J. SEIDE. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **28**, 401–407, Sept.–Oct., 1954. 6 refs.

829. **Doctor and Priest in Pergamon.** (Arzt und Priester in Pergamon)
H. ERHARD. *Gesnerus* [*Gesnerus* (*Aarau*)] **11**, 11–16, 1954.